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SEARCH REQ

Requester's Full Name: Krista Bianchi Date: 9/5/08

Art Unit: 1626 Phone Number: 2-0252 Serial Number: 10/569486

Location (Bldg/Room#): Rem 4 (Mailbox #): N/A Results Format Preferred (circle): PAPER DISK

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To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Process for Producing an aromatic substituted compound

Inventors (please provide full names):

Weiqi Wang & Tetsuya Ikemoto

Earliest Priority Date: 08/22/03

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search Claim 1.

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DICTIONARY FILE UPDATES:    7 SEP 2008  HIGHEST RN 1047406-12-1

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FILE LAST UPDATED: 7 Sep 2008  (20080907/ED)

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=> d stat que L25
L23         30349 SEA FILE=CAPLUS ABB=ON  PLU=ON  WANG W?/AU
L24           645 SEA FILE=CAPLUS ABB=ON  PLU=ON  IKEMOTO T?/AU
L25             8 SEA FILE=CAPLUS ABB=ON  PLU=ON  L23 AND L24


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L24         645 SEA FILE=CAPLUS ABB=ON  PLU=ON  IKEMOTO T?/AU
L25           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  L23 AND L24
L26           9 SEA L25


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L45          10 DUP REM L25 L26 (7 DUPLICATES REMOVED)
                ANSWERS '1-8' FROM FILE CAPLUS
                ANSWERS '9-10' FROM FILE WPIX

=> d ibib abs L45 1-8; d iall L45 9-10

L45  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2007:461305  CAPLUS  Full-text
DOCUMENT NUMBER:          146:462239
TITLE:                    Process for preparation of dibenzoxepinopyrrole
                          compounds and intermediates
INVENTOR(S):              Wang, Weiqi; Ikemoto, Tetsuya
PATENT ASSIGNEE(S):       Sumitomo Chemical Co., Ltd., Japan
SOURCE:                   PCT Int. Appl., 33pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2007046554        A1    20070426    WO 2006-JP321452       20061020
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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KG, KZ, MD, RU, TJ, TM
JP 2007137877 A 20070607 JP 2006-286275 20061020
PRIORITY APPLN. INFO.: JP 2005-307588 A 20051021
OTHER SOURCE(S): CASREACT 146:462239; MARPAT 146:462239
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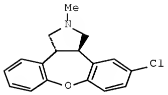

I

AB Disclosed is a process for preparation of compound I and a pharmaceutically acceptable salt thereof in a multi-step synthesis, which comprises intramol. cyclization and reduction Also disclosed is intermediates for the production of the compound I. Further disclosed is a process for production of the intermediates.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2006:787645 CAPLUS Full-text
DOCUMENT NUMBER: 145:230397
TITLE: Preparation of unsaturated (hetero)aromatic compounds having electron-withdrawing group
INVENTOR(S): Wang, Wei-Chi; Ikemoto, Tetsuya
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006206466	A	20060810	JP 2005-17794	20050126

PRIORITY APPLN. INFO.: JP 2005-17794 20050126
OTHER SOURCE(S): MARPAT 145:230397

AB ArCH:CRY [Ar = (un)substituted (hetero)aryl; R = C1-12 linear or branched alkyl; aryl-C1-8 alkyl; Y = electron-withdrawing group], useful as intermediates for drugs and agrochems., are prepared by reacting ArH (Ar = same as above) with ZC:CRY (R, Y = same as above; Z = lower alkoxy) or Z2CCRY (R, Y = same as above; Z = lower alkoxy) in the presence of acids or compds. capable of mineral acids upon hydrolysis. Thus, an AcOH solution of 1,3,5-(MeO)3C6H3 was treated with (MeO)2CHCHBuCO2Et and an aqueous HBr solution under stirring at room temperature overnight to give 67.0% 2,4,6-(MeO)3C6H2CH:CBuCO2Et.

L45 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2006:468875 CAPLUS Full-text
DOCUMENT NUMBER: 144:488633

TITLE: Preparation of antithrombotic clopidogrel
INVENTOR(S): Wang, Wei-Chi; Ikemoto, Tetsuya; Liang, Ting
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006124326	A	20060518	JP 2004-314850	20041028

PRIORITY APPLN. INFO.: JP 2004-314850 20041028
OTHER SOURCE(S): MARPAT 144:488633
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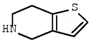
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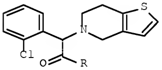
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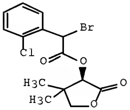

III

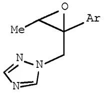
AB Clopidogrel or its pharmaceutically-acceptable salts are prepared by reacting 2-ClC6H4CHXCOR [X = halo, OSO2R1; R1 = lower (halo)alkyl, (un)substituted aryl; R = substituent containing asym. C] with 4,5,6,7-tetrahydrothieno[3,2-c]pyridine (I) and converting the resulting II (R = same as above). Thus, SOCl2 was added dropwise to a toluene solution of 40 g α-bromo-(2-chlorophenyl)acetic acid at room temperature and the reaction mixture was heated at 75° for 3 h. The toluene solution of the resulting acid chloride was added to a THF solution of 24.5 g D-(-)-pantoyl lactone and Et3N at 0-5° and the reaction mixture was stirred fir 1 h to give 39.4 g (R)-4,4-dimethyl-2-oxotetrahydrofuran-3-yl α-bromo-(2-chlorophenyl)acetate (III). A THF solution of 3.26 g I was added dropwise to a THF solution of III, Et3N, and Bu4NI at 0-5° and the reaction mixture was stirred for 1 h to give 67% (R)-4,4-dimethyl-2- oxotetrahydrofuran-3-yl (S)-α-5-(4,5,6,7-tetrahydro[3,2-c]thienopyridyl)-2-chlorophenylacetate. This was treated with a mixture of LiOMe, MeOH, and Me3COMe at 0° for 4 h to give 57% clopidogrel.

L45 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2005:490343 CAPLUS Full-text
DOCUMENT NUMBER: 143:43877
TITLE: Process for producing epoxytriazole compounds and intermediate therefor
INVENTOR(S): Wang, Weiqi; Ikemoto, Tetsuya
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051879	A1	20050609	WO 2004-JP17992	20041126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005154377	A	20050616	JP 2003-398252	20031127
EP 1693358	A1	20060823	EP 2004-819487	20041126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1906146	A	20070131	CN 2004-80040853	20041126
CN 101250163	A	20080827	CN 2008-10081772	20041126
IN 2006CN02344	A	20070706	IN 2006-CN2344	20060626
PRIORITY APPLN. INFO.:			JP 2003-398252 A	20031127
			CN 2004-80040853 A3	20041126
			WO 2004-JP17992 W	20041126

OTHER SOURCE(S): MARPAT 143:43877
GI



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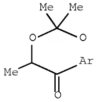

II

AB Process for the preparation of compound I [Ar = difluorophenyl] from compound II [Ar has the same meaning as defined above.] was provided. For example, a

solution of (2R,3R)-3-(2',4'-difluorophenyl)-3,4-ethoxy-2-(1'-methoxy-1'-methylethoxy)butane (34.0 g) in toluene (60 mL), methanol (10 mL) and water (5 mL) was treated with methanesulfonic acid (56 mg) at room temperature for 5 min. Aqueous work-up afforded (2R,3R)-3-(2',4'-difluorophenyl)-2- hydroxy-3,4-epoxybutane (III) (24.5 g). Then, exposure of a mixture of III (24.5 g) in toluene (108 mL) to methanesulfonyl chloride (14.6 g) and triethylamine (13.5 g) at 0-15 ℃ gave (2R,3R)-3-(2',4'- difluorophenyl)-3,4-epoxy-2-methanesulfonyloxybutane (IV) (32.3 g). To a mixture of IV in DMF (35 mL) was added 1,2,4-triazole sodium salt, e.g., in-situ prepared from 1,2,4-triazole (10.4 g) and NaH (5.56 g, 60% in paraffin), over a period of 2 h maintaining 55-65 ℃, the resulting mixture was stirred for addnl. 2 h to furnish compound (2R,3S)-I [Ar = 2,4-difluorophenyl] (13.4 g). Of note, compound I is an useful intermediate for a fungicide.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2005:487859 CAPLUS Full-text
DOCUMENT NUMBER: 143:26493
TITLE: Preparation of syn-1,3-diols by stereoselective reduction
INVENTOR(S): Wang, Wei-Chi; Ikemoto, Tetsuya
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005145833	A	20050609	JP 2003-381816	20031111
PRIORITY APPLN. INFO.:			JP 2003-381816	20031111

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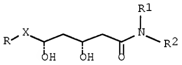

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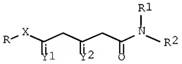

II

AB Title compds. I [X = CH:CH, CH2CH2, OCH2; R = aromatic group having inert group; R1, R2 = lower alkyl; NR1R2 may form (O-containing) nonarom. heterocyclyl], useful as hypolipemic agents (no data), are prepared by (A) mixing R32BOR4 (R3 = lower alkyl; R4 = lower alkyl, aryl) or R53B with NaBH4

in lower alc.-THF mixed solvent system and (B) reduction of keto alcs. II (Y1 or Y2 = O; the other = OH; the broken line may be bond; X, R, R1, R2 = same as above) with the mixts. Preparation of (cyclization products of) carboxylic acids (salts) corresponding to the products is also claimed. Thus, THF-MeOH solution of 7-[3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl]-5- hydroxy-3-oxo-hept-6E-enoic acid dimethylamide was added to THF-MeOH solution containing $NaBH_4$ and Et_2BOMe at -78° over 35 min and the reaction mixture was stirred for 2.5 h to give the corresponding syn-1,3-diol with 79.4% yield.

L45 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2005:378843 CAPLUS Full-text
DOCUMENT NUMBER: 143:78029
TITLE: A practical synthesis of 3-indolyl α,β-unsaturated carbonyl compounds
AUTHOR(S): Wang, Weiqi; Ikemoto, Tetsuya
CORPORATE SOURCE: Fine Chemicals Research Laboratory, Ltd., Sumitomo Chemical Co., Nishiyodogawa-ku, Osaka, 555-0021, Japan
SOURCE: Tetrahedron Letters (2005), 46(22), 3875-3878
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:78029
AB An acid-catalyzed practical synthesis of 3-indolyl α,β-unsatd. carbonyl compds. using Me 3-methoxyacrylate, Me 3,3-dimethoxypropionate, or 1,1-dimethoxy-3-butanone is reported. HCl aqueous solution (35%) catalyzes this reaction efficiently in acetic acid. One of the most favorable substrates is 3-(4-fluorophenyl)-1-isopropyl-1H-indole, which reacts nearly quant. to give the corresponding α,β-unsatd. ester, and the scope of the reaction can be extended to some electron-rich benzene derivs.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2003:1007919 CAPLUS Full-text
DOCUMENT NUMBER: 140:59645
TITLE: Production methods of epoxytriazole derivative and intermediate therefor
INVENTOR(S): Wang, Weiqi; Ikemoto, Tetsuya
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan; Sumitomo Chemical Company, Limited
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030236419	A1	20031225	US 2002-335400	20021231
US 6884892	B2	20050426		
CA 2489611	A1	20031231	CA 2003-2489611	20030610
WO 2004000826	A1	20031231	WO 2003-JP7316	20030610

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PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003242144	A1	20040106	AU 2003-242144		20030610
EP 1535914	A1	20050601	EP 2003-730869		20030610

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CN 1662518	A	20050831	CN 2003-814450		20030610
CN 1970522	A	20070530	CN 2006-10169394		20030610
US 20040267024	A1	20041230	US 2004-842600		20040510
US 7297802	B2	20071120			
IN 2004CN03158	A	20060303	IN 2004-CN3158		20041213
PRIORITY APPLN. INFO.:			JP 2002-180610	A	20020620
			JP 2002-313317	A	20021028
			JP 2002-318833	A	20021031
			US 2002-335400	A3	20021231
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			WO 2003-JP7316	W	20030610

OTHER SOURCE(S): MARPAT 140:59645

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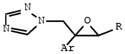
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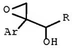
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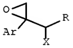
IV

AB An epoxytriazole derivative (I) [wherein Ar is a Ph group optionally substituted by 1 to 3 halogen atom(s) or trifluoromethyl group, R is a hydrogen atom or lower alkyl group] useful as an intermediate for anti-fungal agents and an intermediate therefor having high quality can be produced economically and efficiently by the following industrial means. A compound of the following formula ArCOCH(R)OH (II) (Ar, R = same as above) is reacted with trimethyloxosulfonium salt and the like in the presence of a base to give an epoxide compound (III; Ar, R = same as above) which is converted to the compound (IV; Ar, R = same as above; X is a leaving group) and then reacted with 1,2,4-triazole in the presence of a base. Thus, trimethyloxosulfonium bromide (2.66 g) was dissolved in DMSO (13 mL) and treated with sodium hydride (60 % dispersion in oil, 0.27 g) by small portions at room temperature and then after generation of hydrogen stopped, a solution (5 mL) of (2R)-2',4'-difluoro-2-hydroxypropiophenone (V) (1.10 g) in DMSO slowly and the mixture was stirred for about 30 min to give, after workup, a 12:1 mixture (1.06 g) of (2R,3R)-3-(2',4'-difluorophenyl)-3,4- epoxy-2-butanol and its (2R,3S)-diastereomer. The latter diastereomer mixture (0.3 g) and 0.312 mL Et3N were added to toluene (5 mL), cooled to 0-10°, treated dropwise with methanesulfonyl chloride (0.14 mL), and stirred for 1 h to give, after workup, 0.42 g (2R,3R)-3-(2',4'- difluorophenyl)-3,4-epoxy-2-methanesulfonyloxybutane (VI). To a solution (3 mL) of 1,2,4-triazole (0.259 g) in DMF was added small portions of NaH (60% dispersion in oil, 0.12 g) at .apprx.20° and red for about 3 h until hydrogen was not generated, to give a solution of sodium salt of 1,2,4-triazole thus obtained which was treated dropwise with a solution (5.5 mL) of the total amount of VI obtained above in DMF at room temperature

and stirred at 75-80° for 1.5 h to give, after workup and silica gel chromatog., 0.185 g (2S,3R)-2-(2,4-difluorophenyl)-3-methyl-2-[(1H-1,2,4-triazol-1-yl)methyl]oxirane (44% yield). The reaction of the compound II (not protected) with trimethyloxosulfonium salt and the like surprisingly proceeded easily to give compound III. When compound II was in an optically active form, e.g. V, induction of racemization in this reaction was worried, but racemization was not observed in most cases. The use of compound II resulted in strikingly improved diastereoselectivity as compared to the use of a compound protected by tetrahydropyranyl group. Moreover, the epoxytriazole derivative I could be synthesized efficiently from the compound IV, which was produced by substituting the hydroxy group in compound III for a leaving group.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:806468 CAPLUS Full-text

DOCUMENT NUMBER: 149:104674

TITLE: Process for producing intermediate of asenapine synthesis

INVENTOR(S): Tokuda, Osamu; Wang, Weiqi; Ikemoto, Tetsuya

PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan

SOURCE: PCT Int. Appl., 17pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008078482	A1	20080703	WO 2007-JP72601	20071115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2008174547	A	20080731	JP 2007-313406	20071204

PRIORITY APPLN. INFO.: JP 2006-346735 A 20061222

AB Disclosed is a process for producing 2-(2-(4-chlorophenoxy)phenyl)acetic acid by reaction of (2-chlorophenyl)acetic acid with 4-chlorophenol. Thus, a mixture of (2-chlorophenyl)acetic acid (1.00 g), 4-chlorophenol (0.78 g), Cs_2CO_3 (3.80 g) and CuBr (42 mg) in diethyleneglycol di-Me ether (5 mL) was stirred at 145° for 8 h. After cooling and adjusting pH using HCl, the resulting reaction mixture was extracted with toluene. The organic layer was washed with brine, dried over $MgSO_4$ and filtered to give a solution of 2-(2-(4-chlorophenoxy)phenyl)acetic acid in toluene (59% yield).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 9 OF 10 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 2005-233057 [24] WPIX Full-text
DOC. NO. CPI: C2005-073858 [24]
TITLE: Synthesis of aromatic unsaturated compound useful as synthetic intermediate in pharmaceuticals, involves reacting specific aromatic compound with unsaturated compound in presence of compound producing mineral acid on hydrolysis
DERWENT CLASS: B05; C03
INVENTOR: IKEMOTO T; O I; WANG W; WENG W
PATENT ASSIGNEE: (SUMO-C) SUMITOMO CHEM CO LTD
COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005021465	A1	20050310	(200524)*	JA	35[0]	
JP 2005097227	A	20050414	(200527)	JA	18	
EP 1666440	A1	20060607	(200638)	EN		
CN 1871188	A	20061129	(200720)	ZH		
KR 2007000387	A	20070102	(200755)	KO		
IN 2006CN01042	P4	20070629	(200768)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005021465	A1	WO 2004-JP12601	20040825
JP 2005097227	A	JP 2003-384566	20031114
CN 1871188	A	CN 2004-80030885	20040825
EP 1666440	A1	EP 2004-772557	20040825
EP 1666440	A1	WO 2004-JP12601	20040825
KR 2007000387	A	WO 2004-JP12601	20040825
IN 2006CN01042	P4	WO 2004-JP12601	20040825
KR 2007000387	A	KR 2006-703787	20060224
IN 2006CN01042	P4	IN 2006-CN1042	20060327

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1666440	A1	Based on	WO 2005021465	A
KR 2007000387	A	Based on	WO 2005021465	A

PRIORITY APPLN. INFO: JP 2003-384566 20031114
JP 2003-209042 20030827

INT. PATENT CLASSIF.:
MAIN: C07B037-04
IPC ORIGINAL: C07B0037-00 [I,C]; C07B0037-00 [I,C]; C07B0037-04 [I,A]; C07C0067-00 [I,C]; C07C0067-00 [I,C]; C07C0067-343 [I,A]; C07C0067-343 [I,A]; C07C0069-00 [I,C]; C07C0069-734 [I,A] ; C07D0209-10 [I,A]; C07D0209-24 [I,A]
IPC RECLASSIF.: C07B0037-00 [I,C]; C07B0037-04 [I,A]; C07B0061-00 [I,A]; C07B0061-00 [I,C]; C07C0067-00 [I,C]; C07C0067-32 [I,A]; C07C0067-343 [I,A]; C07C0069-00 [I,C]; C07C0069-736 [I,A] ; C07D0209-00 [I,C]; C07D0209-08 [I,A]; C07D0209-10 [I,A] ; C07D0209-12 [I,A]; C07D0209-18 [I,A]; C07D0209-24 [I,A]
ECLA: C07B0037-04; C07C0067-343+69/734; C07D0209-08; C07D0209-10; C07D0209-12; C07D0209-18; C07D0209-24

BASIC ABSTRACT:

WO 2005021465 A1 UPAB: 20071024

NOVELTY - Aromatic compound (1) is reacted with unsaturated compound (2) or (3) in presence of acid or compound producing a mineral acid on hydrolysis, to obtain aromatic unsaturated compound (4).

DETAILED DESCRIPTION - The synthesis of aromatic unsaturated compound of formula (4) involves reacting aromatic compound of formula (1) with unsaturated compound of formula (2) or (3) in presence of acid or a compound producing mineral acid on hydrolysis.

Ar = optionally substituted aromatic/hetero aromatic;

Y = electron attractive group; and

Z = lower alkoxy.

USE - As synthetic intermediate in pharmaceuticals and agrochemicals.

ADVANTAGE - The method enables effective synthesis of aromatic unsaturated compound. The method is simple, economical, eco-friendly in nature and has high industrial utility. MANUAL CODE: CPI: B06-D01; B06-H; B07-H; B10-J02; C06-D01; C06-H;
C07-H; C10-J02

L45 ANSWER 10 OF 10 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN

ACCESSION NUMBER: 2005-074259 [08] WPIX Full-text

CROSS REFERENCE: 2004-120199

DOC. NO. CPI: C2005-025302 [08]

TITLE: Preparation of epoxy derivative, for preparation of epoxytriazole derivative useful synthetic intermediate for anti-fungal agents, involves reacting aryl derivative with trimethyloxosulfonium or trimethylsulfonium salt in presence of base

DERWENT CLASS: B03; C02

INVENTOR: IKEMOTO T; WANG W

PATENT ASSIGNEE: (SUMO-C) SUMIKA FINE CHEM CO LTD; (SUMO-C) SUMITOMO CHEM CO LTD

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20040267024	A1	20041230	(200508)*	EN	13[0]	
US 7297802	B2	20071120	(200778)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20040267024	A1 Div Ex	US 2002-335400	20021231
US 20040267024	A1	US 2004-842600	20040510
US 7297802	B2 Div Ex	US 2002-335400	20021231
US 7297802	B2	US 2004-842600	20040510

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
US 7297802	B2	Div ex	US 6884892	B

PRIORITY APPLN. INFO: JP 2002-318833 20021031
JP 2002-180610 20020620
JP 2002-313317 20021028

INT. PATENT CLASSIF.:

IPC ORIGINAL: C07D0303-00 [I,A]; C07D0303-00 [I,C]
IPC RECLASSIF.: C07D0257-00 [I,C]; C07D0257-02 [I,A]; C07D0405-00 [I,C]; C07D0405-06 [I,A]
ECLA: C07D0405-06
USCLASS NCLM: 548/252.000
BASIC ABSTRACT:

US 20040267024 A1 UPAB: 20050707

NOVELTY - Preparation of epoxy derivative involves reacting aryl derivative with a trimethyloxosulfonium salt or a trimethylsulfonium salt in the presence of a base.

DETAILED DESCRIPTION - Preparation of epoxy derivative of formula (II) involves reacting aryl derivative of formula Ar-C(O)-C(R)-OH (I) with a trimethyloxosulfonium salt or a trimethylsulfonium salt in the presence of a base.

Ar = phenyl (optionally mono- - tri-substituted by halo or trifluoromethyl) (preferably 2,4-difluorophenyl);

R = H or lower alkyl (preferably methyl).

INDEPENDENT CLAIMS are included for the following:

(1) preparation of aryltriazole derivative of formula (III) or its salt involving preparing (II) and reacting with 1,2,4-triazole in the presence of base;

(2) preparation of epoxyaryl derivative of formula (IV) involving preparing (II) and converting to (IV);

(3) intermediate (2R)-2-(1-Ethoxyethoxy)-1-(2,4-difluorophenyl)-1-propanone.

X = leaving group.

USE - For preparation of epoxytriazole derivative e.g. 1-(2-(2,4-difluoro-phenyl)-3-methyl-oxiranylmethyl)-1H-(1,2,4)triazole, useful synthetic intermediate for anti-fungal agents such as triazole compounds.

ADVANTAGE - The epoxytriazole derivative, useful synthetic intermediate for anti-fungal agents having high quality can be produced economically and efficiently industrially. The epoxidation proceeds even without protecting deprotected 1-(2,4-difluoro-phenyl)-2-(tetrahydro- pyran-2-yloxy)-propan-1-one. The diastereoselectivity is dramatically improved.

MANUAL CODE: CPI: B07-A03; B07-D13; C07-A03; C07-D13

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FILE CONTENT:1840 - 31 Aug 2008 VOL 149 ISS 10

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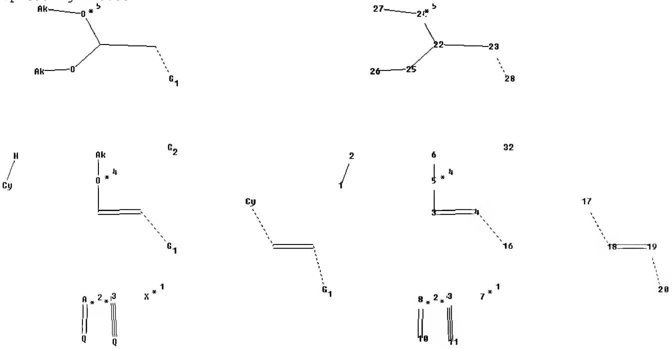

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chain nodes :
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1  2  3  4  5  6  7  16  17  18  19  20  22  23  24  25  26  27  28  32
ring/chain nodes :
8  9  10  11
chain bonds :
1-2  3-4  3-5  4-16  5-6  17-18  18-19  19-20  22-23  22-24  22-25  23-28  24-27
25-26
ring/chain bonds :
8-10  9-11
exact/norm bonds :
1-2  3-5  4-16  5-6  8-10  9-11  17-18  19-20  22-24  22-25  23-28  24-27  25-26

exact bonds :
3-4  18-19  22-23


G1:[*1],[*2],[*3]

G2:[*4],[*5]

Match level :
1:Atom  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS
11:CLASS  16:CLASS  17:Atom  18:CLASS  19:CLASS  20:CLASS  22:CLASS  23:CLASS
24:CLASS  25:CLASS
26:CLASS  27:CLASS  28:CLASS  32:CLASS
Generic attributes :
1:
Saturation             : Unsaturated
17:
Saturation             : Unsaturated

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containing 32
fragments assigned product role:
containing 17
reaction site bonds:
17-18:CC



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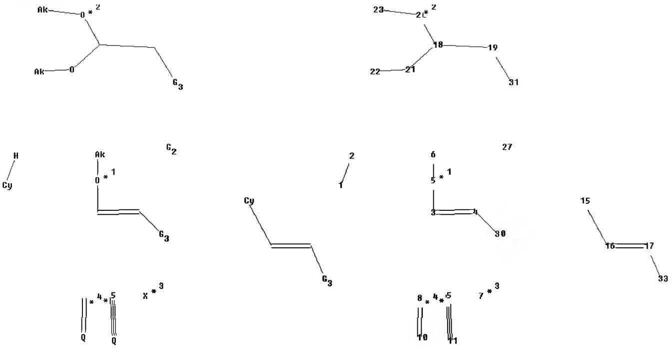

chain nodes :
1 2 3 4 5 6 7 8 9 10 11 15 16 17 18 19 20 21 22 23 27 30 31
33
chain bonds :
1-2 3-4 3-5 4-30 5-6 8-10 9-11 15-16 16-17 17-33 18-19 18-20 18-21 19-
31
20-23 21-22
exact/norm bonds :
1-2 3-5 4-30 5-6 8-10 9-11 15-16 17-33 18-20 18-21 19-31 20-23 21-22

exact bonds :
3-4 16-17 18-19

G2:[*1],[*2]

G3:[*3],[*4],[*5]

Hydrogen count :
3:= exact 1 4:= exact 1 16:= exact 1 17:= exact 1 18:= exact 1 19:= exact 2

Connectivity :
3:2 E exact RC ring/chain 4:2 E exact RC ring/chain 16:2 E exact RC ring/chain
17:2 E exact RC ring/chain 18:3 E exact RC ring/chain 19:2 E exact RC ring/chain
Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS
11:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS
27:CLASS 30:CLASS 31:CLASS 33:CLASS
Generic attributes :
1:
Saturation : Unsaturated
15:
Saturation : Unsaturated

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fragments assigned reactant role:
containing 1
containing 27
fragments assigned product role:
containing 15
reaction site bonds:
15-16:CC



=> d stat que L14
L1                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L2   (    190274)SEA FILE=CASREACT ABB=ON  PLU=ON  ACYCLIC ALKENE/FG.PRO
L3                SCR 278 OR 1342
L4            143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 (   742 REACTIONS)
L5                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L7             43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 (   207 REACTIONS)
L8                TRANSFER  PLU=ON  L4 1- RX :    1312 TERMS
L9           1312 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8/RN
L10           441 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND X/ELS
L11           421 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND C/ELS
L12            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 NOT L11
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Structure attributes must be viewed using STN Express query preparation.
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L3                SCR 278 OR 1342
L4            143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 (   742 REACTIONS)
L5                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
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L8                TRANSFER  PLU=ON  L4 1- RX :    1312 TERMS
L9           1312 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8/RN
L10           441 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND X/ELS
L11           421 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND C/ELS
L12            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 NOT L11
L13        188275 SEA FILE=CASREACT ABB=ON  PLU=ON  L12
L14            24 SEA FILE=CASREACT ABB=ON  PLU=ON  L13 (L) L7
L37         75833 SEA FILE=CASREACT ABB=ON  PLU=ON  64-19-7
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=> d stat que L21
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
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L3              SCR 278 OR 1342
L4           143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 (   742 REACTIONS)
L5              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L7           43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 (   207 REACTIONS)
L8              TRANSFER  PLU=ON  L4 1- RX :    1312 TERMS
L9          1312 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8/RN
L10          441 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND X/ELS
L11          421 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND C/ELS
L12           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 NOT L11
L13       188275 SEA FILE=CASREACT ABB=ON  PLU=ON  L12
L14           24 SEA FILE=CASREACT ABB=ON  PLU=ON  L13 (L) L7
L16           11 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND M/ELS
L17            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 NOT L16
L18       153759 SEA FILE=CASREACT ABB=ON  PLU=ON  L17
L19           31 SEA FILE=CASREACT ABB=ON  PLU=ON  L18 (L) L4
L21           15 SEA FILE=CASREACT ABB=ON  PLU=ON  L19 AND L14


=> s L14 or L40 or L21
L46          24 L14 OR L40 OR L21

=> d ibib abs hit L46 1-24


L46  ANSWER 1 OF 24  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         148:262034  CASREACT  Full-text
TITLE:                    Synthesis and structure of polyunsaturated
                          [10]paracyclophane annulated by two azulene rings
AUTHOR(S):                Kuroda, Shigeyasu; Obata, Yuji; Thanh, Nguyen Chung;
                          Miyatake, Ryuta; Horino, Yoshikazu; Oda, Mitsunori
CORPORATE SOURCE:         Department of Applied Chemistry, Graduate School of
                          Science and Engineering, University of Toyama, Toyama,
                          930-8555, Japan
SOURCE:                   Tetrahedron Letters (2008), 49(3), 552-556
                          CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER:                Elsevier Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
GI
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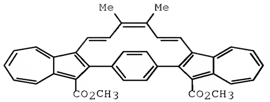
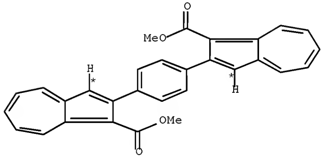


I

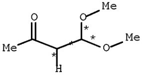
AB The polyunsatd. [10]cyclophane I was synthesized from 1,4-diacetylbenzene by a four-step sequence involving the modified Yasunami azulene synthesis, introduction of two butenone units, and a subsequent McMurry coupling reaction. The crystal structures of I and a synthetic intermediate were determined by X-ray crystallog. anal. The results revealed that (1) the benzene ring of I is distorted as a boat form with relatively small bending angles and (2) the azulene rings of the intermediate show large out-of-plane deformation along the short azulene mol. axis.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 6 ...C + 2 E ===> F...

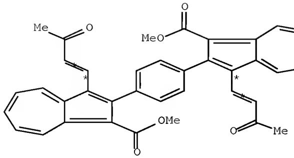


C



2 E

(2) →



F
YIELD 28%

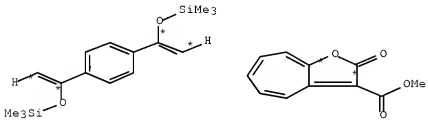
RX(2)   RCT C 1006389-39-4, E 5436-21-5

  STAGE(1)
    RGT G 16872-11-0 HBF4

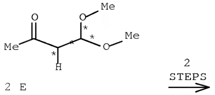
  STAGE(2)
    RGT H 497-19-8 Na2CO3

PRO F 1006389-40-7
NTE stereoselective

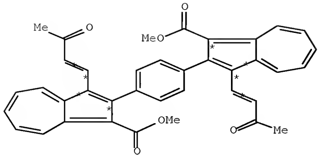
RX(4) OF 6 COMPOSED OF RX(1), RX(2)
RX(4)   A + 2 B + 2 E ===> F



A   2 B



2 E



F
YIELD 28%

```
RX(1)      RCT  A 183060-22-2, B 50603-71-9
           PRO  C 1006389-39-4
           SOL  91-17-8 Decalin
           CON  4 hours, reflux
           NTE  modified TYasunami-Takase azulene reaction

RX(2)      RCT  C 1006389-39-4, E 5436-21-5

             STAGE(1)
                RGT  G 16872-11-0 HBF4

             STAGE(2)
                RGT  H 497-19-8 Na2CO3

           PRO  F 1006389-40-7
           NTE  stereoselective
```

L46 ANSWER 2 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 143:153252 CASREACT Full-text

TITLE: A convenient synthesis and chemical properties of 3-acylamino-6-polyfluoroalkyl-2H-pyran-2-ones

AUTHOR(S): Gerus, Igor I.; Tolmachova, Nataliya A.; Vdovenko, Sergey I.; Froehlich, Roland; Haufe, Guenter

CORPORATE SOURCE: Institute of Bioorganic Chemistry and Petrochemistry NASU, Kiev, 02094, Ukraine

SOURCE: Synthesis (2005), (8), 1269-1278
CODEN: SYNTBF; ISSN: 0039-7881

PUBLISHER: Georg Thieme Verlag

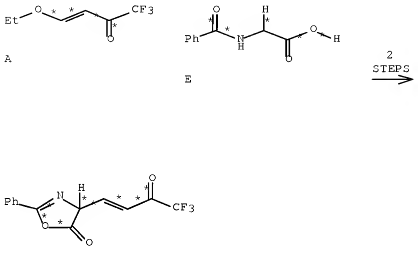
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A number of 3-acylamino-6-polyfluoroalkyl-2H-pyran-2-ones were synthesized from β-alkoxyvinyl polyfluoroalkyl ketones and N-acylglycines in acetic anhydride in high yield. The reactions of 6-trifluoromethyl-3- benzoylamino-2H-pyran-2-one with O- and N-nucleophiles were studied and 3-N-benzoylamino-6-hydroxy-6-trifluoromethyl-5,6-dihydro-2H-pyran-2-one,3- N-benzoylamino-6-hydroxy-6-trifluoromethyl-5,6-dihydro-2H-pyridin-2-one, and N- and O-substituted 3-(N-benzoylamino)-6-trifluoromethyl-2H-pyridin-2- ones were synthesized.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(30) OF 53 COMPOSED OF RX(2), RX(12)
RX(30)   A + E ===> Y



Y
YIELD 93%

RX(2)   RCT A 17129-06-5, E 495-69-2
          PRO F 312615-59-1
          SOL 108-24-7 Ac2O
          CON 6 hours, 60 deg C

RX(12)   RCT F 312615-59-1

STAGE(1)
RGT Z 1310-58-3 KOH
SOL 68-12-2 DMF
CON 2 hours, 60 deg C

STAGE(2)
RGT AA 7647-01-0 HCl
SOL 7732-18-5 Water
CON pH 3

PRO Y 860454-19-9

L46 ANSWER 3 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

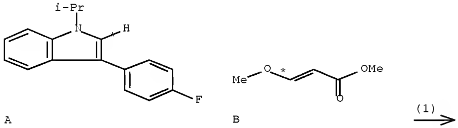
ACCESSION NUMBER: 143:78029 CASREACT Full-text
TITLE: A practical synthesis of 3-indolyl α,β-unsaturated carbonyl compounds
AUTHOR(S): Wang, Weiqi; Ikemoto, Tetsuya
CORPORATE SOURCE: Fine Chemicals Research Laboratory, Ltd., Sumitomo Chemical Co., Nishiyodogawa-ku, Osaka, 555-0021, Japan
SOURCE: Tetrahedron Letters (2005), 46(22), 3875-3878
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal

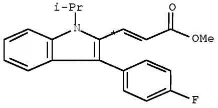
LANGUAGE: English

AB An acid-catalyzed practical synthesis of 3-indolyl α,β-unsatd. carbonyl compds. using Me 3-methoxyacrylate, Me 3,3-dimethoxypropionate, or 1,1-dimethoxy-3-butanone is reported. HCl aqueous solution (35%) catalyzes this reaction efficiently in acetic acid. One of the most favorable substrates is 3-(4-fluorophenyl)-1-isopropyl-1H-indole, which reacts nearly quant. to give the corresponding α,β-unsatd. ester, and the scope of the reaction can be extended to some electron-rich benzene derivs.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 11 A + B ===> C

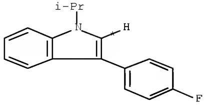




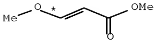
C
YIELD 94%

RX(1)	RCT	A 93957-49-4, B 5788-17-0
	PRO	C 145797-77-9
	CAT	7647-01-0 HCl
	SOL	7732-18-5 Water, 64-19-7 AcOH
	CON	15 hours, 25 deg C
	NTE	optimization study, similar yield is obtained with POCl3 as a catalyst

RX(2) OF 11 A + B ===> C

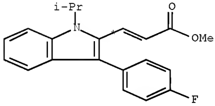


A



B

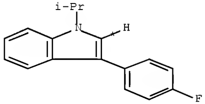
(2) →



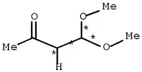
C
YIELD 95%

```
RX(2)       RCT  A 93957-49-4, B 5788-17-0
            PRO  C 145797-77-9
            CAT  10025-87-3 POCl3
            SOL  7732-18-5 Water, 64-19-7 AcOH
            CON  9 hours, 25 deg C
            NTE  optimization study, optimized on catalyst and solvent

RX(3) OF 11     A  +  H  ===>  I
```

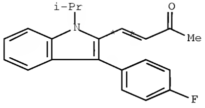


A



H

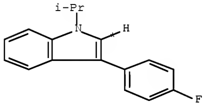
(3) →



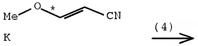
I
YIELD 50%

RX(3)   RCT A 93957-49-4, H 5436-21-5
           PRO I 847646-86-0
           CAT 7647-01-0 HCl
           SOL 7732-18-5 Water, 64-18-6 HCO2H
           CON 18 hours, 25 deg C

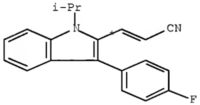
RX(4) OF 11   A + K ===> L



A



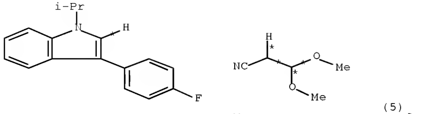
K



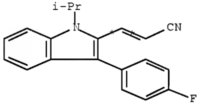
L
YIELD 36%

RX(4)   RCT A 93957-49-4, K 69194-03-2
           PRO L 847646-85-9
           CAT 10025-87-3 POCl3
           SOL 7732-18-5 Water, 64-19-7 AcOH
           CON 15 hours, 25 deg C

RX(5) OF 11 A + M ===> L



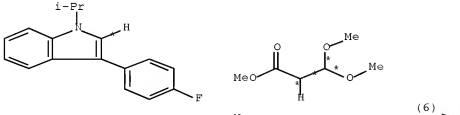
A M



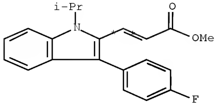
L
YIELD 25%

```
RX(5)      RCT  A 93957-49-4, M 57597-62-3
           PRO  L 847646-85-9
           CAT  7647-01-0 HCl
           SOL  7732-18-5 Water, 64-19-7 AcOH
           CON  18 hours, 25 deg C
```

RX(6) OF 11 A + N ===> C



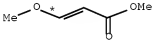
A N



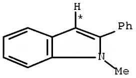
C
YIELD 95%

RX(6)   RCT A 93957-49-4, N 7424-91-1
           RGT O 108-24-7 Ac2O
           PRO C 145797-77-9
           CAT 10035-10-6 HBr
           SOL 64-19-7 AcOH
           CON 5 hours, 25 deg C

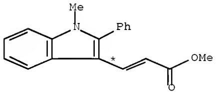
RX(7) OF 11   B + Q ===> R



B



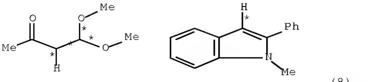
Q



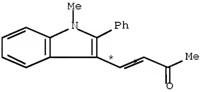
R
YIELD 82%

RX(7)   RCT B 5788-17-0, Q 3558-24-5
           PRO R 141854-06-0
           CAT 10025-87-3 POCl3
           SOL 7732-18-5 Water, 64-19-7 AcOH
           CON 7 hours, 25 deg C

RX(8) OF 11 H + Q ===> S



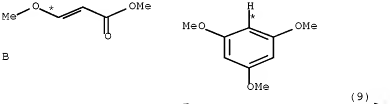
H Q



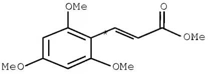
S
YIELD 89%

RX(8)	RCT	H 5436-21-5, Q 3558-24-5
	PRO	S 847646-87-1
	CAT	7647-01-0 HCl
	SOL	7732-18-5 Water, 64-19-7 AcOH
	CON	14 hours, 25 deg C

RX(9) OF 11 B + T ===> U



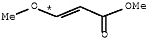
B T



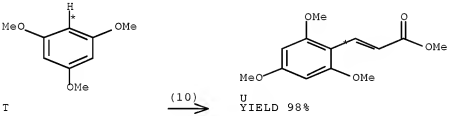
U
YIELD 92%

```
RX(9)       RCT  B 5788-17-0, T 621-23-8
            PRO  U 847646-83-7
            CAT  10025-87-3 POCl3
            SOL  7732-18-5 Water, 64-19-7 AcOH
            CON  5 hours, 25 deg C
            NTE  HCl a a catalyst provided higher yield
```

RX(10) OF 11   B + T ===> U



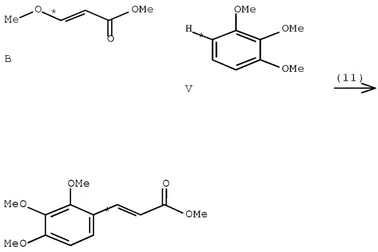
B



T (10) U
YIELD 98%

```
RX(10)      RCT  B 5788-17-0, T 621-23-8
            PRO  U 847646-83-7
            CAT  7647-01-0 HCl
            SOL  7732-18-5 Water, 64-19-7 AcOH
            CON  1 hour, 25 deg C
```

RX(11) OF 11   B + V ===> W



B

V

(11)

W
YIELD 25%

```
RX(11)     RCT  B 5788-17-0, V 634-36-6
           PRO  W 116406-21-4
           CAT  10025-87-3 POCl3
           SOL  7732-18-5 Water, 64-19-7 AcOH
           CON  18 hours, 25 deg C
```

L46 ANSWER 4 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 140:16915 CASREACT Full-text

TITLE: Synthesis and Biological Evaluation of 5-Substituted Derivatives of the Potent Antiherpes Agent (north)-Methanocarbathymine

AUTHOR(S): Russ, Pamela; Schelling, Pierre; Scapozza, Leonardo; Folkers, Gerd; De Clercq, Erik; Marquez, Victor E.

CORPORATE SOURCE: Laboratory of Medicinal Chemistry, Center for Cancer Research, National Cancer Institute at Frederick, Frederick, MD, 21702, USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(23), 5045-5054
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

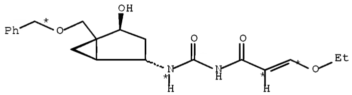
LANGUAGE: English

AB The conformationally locked nucleoside, (north)-methanocarbathymine, is a potent and selective anti-herpes agent effective against herpes simplex type 1 (HSV1) and type 2 (HSV2) viruses. Here we report on the synthesis and biol. evaluation of a small set of 5-substituted pyrimidine nucleosides belonging to the same class of bicyclo[3.1.0]hexane nucleosides. Both the 5-bromovinyl and the 5-bromo analog appeared to be exclusive substrates of HSV1 thymidine kinase (TK), contrasting with the 5-iodo analog, which was significantly phosphorylated by the human cytosolic TK. The binding affinity constant and catalytic turnover for HSV1 TK were measured to assess the influence of the substitution on these parameters. In the plaque reduction and cytotoxicity assays, the 5-bromo analog showed good activity against HSV1 and HSV2 with less general toxicity than (north)-methanocarbathymine. Against varicella-zoster virus (VZV), the north-locked 5-bromovinyl analog proved to be as

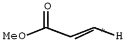
potent as its conformationally unlocked 2'-deoxyriboside equivalent BVDU. The three compds. were also tested in vitro as prodrugs used in a gene therapy context on three osteosarcoma cell lines, either deficient in TK (TK-), nontransduced, or stably transduced with HSV1 TK. The 5-iodo compound (CC50 25 ± 7 μM) was more efficient than ganciclovir (GCV, CC50 75 ± 35 μM) in inhibiting growth of HSV1-TK transfected cells and less inhibitory than GCV toward TK- cells, whereas the 5-bromo compound inhibited transfected and nontransfected cell lines in a relatively similar dose-dependent manner.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(42) OF 63 COMPOSED OF RX(5), RX(6), RX(8), RX(15)
RX(42) T + AX ===> AE

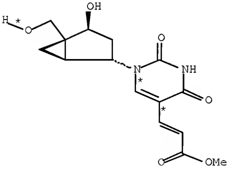


T



AX

4
STEPS
→



AE
YIELD 48%

RX(5) RCT T 391679-36-0

STAGE(1)
RGT V 7664-93-9 H2SO4

```
              SOL  7732-18-5 Water, 64-17-5 EtOH
              CON  1 hour, reflux

           STAGE(2)
              RGT  D 1310-73-2 NaOH
              SOL  7732-18-5 Water
              CON  neutralized

          PRO  U 391679-37-1

RX(6)     RCT  U 391679-37-1
          RGT  Y 7553-56-2 I2, Z 7697-37-2 HNO3
          PRO  X 391679-39-3
          SOL  7732-18-5 Water, 123-91-1 Dioxane
          CON  1 hour, 100 deg C
          NTE  regioselective

RX(8)     RCT  X 391679-39-3

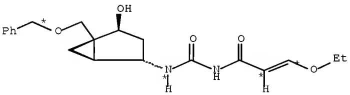
           STAGE(1)
              RGT  R 10294-34-5 BCl3
              SOL  75-09-2 CH2Cl2
              CON  1 hour, -78 deg C

           STAGE(2)
              SOL  67-56-1 MeOH

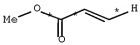
          PRO  Q 391679-34-8

RX(15)    RCT  AX 96-33-3, Q 391679-34-8
          RGT  AY 121-44-8 Et3N
          PRO  AE 391679-42-8
          CAT  3375-31-3 Pd(OAc)2, 603-35-0 PPh3
          SOL  123-91-1 Dioxane
          CON  4 hours, 78 deg C
          NTE  stereoselective


RX(58) OF 63 COMPOSED OF RX(5), RX(6), RX(8), RX(15), RX(10), RX(11)
RX(58)    T  +  AX  ===>  AI
```

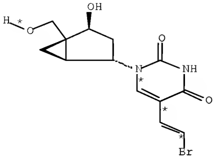


T



AX

6
STEPS



AI
YIELD 25%

```
RX(5)     RCT  T 391679-36-0

            STAGE(1)
               RGT  V 7664-93-9 H2SO4
               SOL  7732-18-5 Water, 64-17-5 EtOH
               CON  1 hour, reflux

            STAGE(2)
               RGT  D 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  neutralized

          PRO  U 391679-37-1

RX(6)     RCT  U 391679-37-1
          RGT  Y 7553-56-2 I2, Z 7697-37-2 HNO3
          PRO  X 391679-39-3
          SOL  7732-18-5 Water, 123-91-1 Dioxane
          CON  1 hour, 100 deg C
          NTE  regioselective

RX(8)     RCT  X 391679-39-3

            STAGE(1)
               RGT  R 10294-34-5 BCl3
               SOL  75-09-2 CH2Cl2
               CON  1 hour, -78 deg C

            STAGE(2)
               SOL  67-56-1 MeOH

          PRO  Q 391679-34-8

RX(15)    RCT  AX 96-33-3, Q 391679-34-8
          RGT  AY 121-44-8 Et3N
          PRO  AE 391679-42-8
          CAT  3375-31-3 Pd(OAc)2, 603-35-0 PPh3
          SOL  123-91-1 Dioxane
          CON  4 hours, 78 deg C
```

NTE stereoselective

RX(10) RCT AE 391679-42-8

STAGE(1)
RGT AG 1310-58-3 KOH
SOL 7732-18-5 Water
CON overnight, room temperature

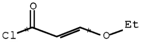
STAGE(2)
RGT AH 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 2

STAGE(3)
SOL 67-56-1 MeOH

PRO AF 391679-43-9

RX(11) RCT AF 391679-43-9
RGT AJ 298-14-6 KHCO3, AK 128-08-5 Bromosuccinimide
PRO AI 391679-35-9
SOL 68-12-2 DMF
CON 2.5 hours, room temperature

RX(59) OF 63 COMPOSED OF RX(14), RX(5), RX(6), RX(8), RX(15), RX(10), RX(11)
RX(59) AT + AU + AV + AX ===> AI



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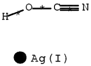

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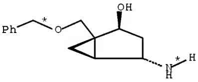

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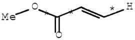

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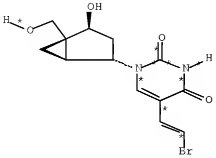


AI
YIELD 25%

RX(14)   RCT AT 6191-99-7, AU 3315-16-0

    STAGE(1)
        SOL 71-43-2 Benzene
        CON SUBSTAGE(1) 2 hours, 100 deg C
             SUBSTAGE(2) 45 minutes, reflux
             SUBSTAGE(3) reflux -> room temperature

    STAGE(2)
        RCT AV 191480-80-5
        SOL 68-12-2 DMF
        CON SUBSTAGE(1) 0 deg C
             SUBSTAGE(2) overnight, 0 deg C -> room temperature

    PRO T 391679-36-0

RX(5)   RCT T 391679-36-0

    STAGE(1)
        RGT V 7664-93-9 H2SO4
        SOL 7732-18-5 Water, 64-17-5 EtOH
        CON 1 hour, reflux

    STAGE(2)
        RGT D 1310-73-2 NaOH
        SOL 7732-18-5 Water
        CON neutralized

    PRO U 391679-37-1

RX(6)   RCT U 391679-37-1
          RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3
          PRO X 391679-39-3
          SOL 7732-18-5 Water, 123-91-1 Dioxane
          CON 1 hour, 100 deg C
          NTE regioselective

RX(8)   RCT X 391679-39-3

    STAGE(1)
        RGT R 10294-34-5 BCl3
        SOL 75-09-2 CH2Cl2

```
                CON  1 hour, -78 deg C

             STAGE(2)
                SOL  67-56-1 MeOH

          PRO  Q 391679-34-8

RX(15)    RCT  AX 96-33-3, Q 391679-34-8
          RGT  AY 121-44-8 Et3N
          PRO  AE 391679-42-8
          CAT  3375-31-3 Pd(OAc)2, 603-35-0 PPh3
          SOL  123-91-1 Dioxane
          CON  4 hours, 78 deg C
          NTE  stereoselective

RX(10)    RCT  AE 391679-42-8

             STAGE(1)
                RGT  AG 1310-58-3 KOH
                SOL  7732-18-5 Water
                CON  overnight, room temperature

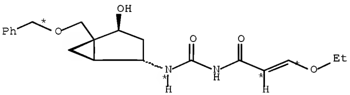
             STAGE(2)
                RGT  AH 7647-01-0 HCl
                SOL  7732-18-5 Water
                CON  room temperature, pH 2

             STAGE(3)
                SOL  67-56-1 MeOH

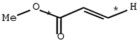
          PRO  AF 391679-43-9

RX(11)    RCT  AF 391679-43-9
          RGT  AJ 298-14-6 KHCO3, AK 128-08-5 Bromosuccinimide
          PRO  AI 391679-35-9
          SOL  68-12-2 DMF
          CON  2.5 hours, room temperature

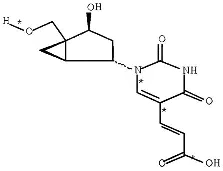

RX(60) OF 63 COMPOSED OF RX(5), RX(6), RX(8), RX(15), RX(10)
RX(60)    T  +  AX  ===>  AF
```



T



AX



AF
YIELD 87%

```
RX(5)     RCT  T 391679-36-0

            STAGE(1)
               RGT  V 7664-93-9 H2SO4
               SOL  7732-18-5 Water, 64-17-5 EtOH
               CON  1 hour, reflux

            STAGE(2)
               RGT  D 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  neutralized

          PRO  U 391679-37-1

RX(6)     RCT  U 391679-37-1
          RGT  Y 7553-56-2 I2, Z 7697-37-2 HNO3
          PRO  X 391679-39-3
          SOL  7732-18-5 Water, 123-91-1 Dioxane
          CON  1 hour, 100 deg C
          NTE  regioselective

RX(8)     RCT  X 391679-39-3

            STAGE(1)
               RGT  R 10294-34-5 BCl3
               SOL  75-09-2 CH2Cl2
               CON  1 hour, -78 deg C

            STAGE(2)
               SOL  67-56-1 MeOH

          PRO  Q 391679-34-8

RX(15)    RCT  AX 96-33-3, Q 391679-34-8
          RGT  AY 121-44-8 Et3N
          PRO  AE 391679-42-8
          CAT  3375-31-3 Pd(OAc)2, 603-35-0 PPh3
```

```
          SOL  123-91-1 Dioxane
          CON  4 hours, 78 deg C
          NTE  stereoselective

RX(10)    RCT  AE 391679-42-8

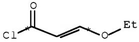
            STAGE(1)
               RGT  AG 1310-58-3 KOH
               SOL  7732-18-5 Water
               CON  overnight, room temperature

            STAGE(2)
               RGT  AH 7647-01-0 HCl
               SOL  7732-18-5 Water
               CON  room temperature, pH 2

            STAGE(3)
               SOL  67-56-1 MeOH

          PRO  AF 391679-43-9


RX(61) OF 63 COMPOSED OF RX(14), RX(5), RX(6), RX(8), RX(15), RX(10)
RX(61)    AT  +  AU  +  AV  +  AX  ===>  AF
```



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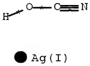
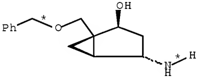
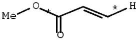


AU

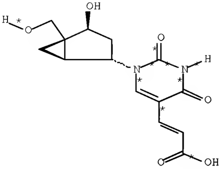


AV



AX

6 STEPS



AF
YIELD 87%

RX(14)   RCT AT 6191-99-7, AU 3315-16-0

  STAGE(1)
    SOL 71-43-2 Benzene
    CON SUBSTAGE(1) 2 hours, 100 deg C
         SUBSTAGE(2) 45 minutes, reflux
         SUBSTAGE(3) reflux -> room temperature

  STAGE(2)
    RCT AV 191480-80-5
    SOL 68-12-2 DMF
    CON SUBSTAGE(1) 0 deg C
         SUBSTAGE(2) overnight, 0 deg C -> room temperature

PRO T 391679-36-0

RX(5)   RCT T 391679-36-0

  STAGE(1)
    RGT V 7664-93-9 H2SO4
    SOL 7732-18-5 Water, 64-17-5 EtOH
    CON 1 hour, reflux

  STAGE(2)
    RGT D 1310-73-2 NaOH
    SOL 7732-18-5 Water
    CON neutralized

PRO U 391679-37-1

RX(6)   RCT U 391679-37-1
RGT Y 7553-56-2 I2, Z 7697-37-2 HNO3
PRO X 391679-39-3
SOL 7732-18-5 Water, 123-91-1 Dioxane
CON 1 hour, 100 deg C
NTE regioselective

RX(8)   RCT X 391679-39-3

  STAGE(1)
    RGT R 10294-34-5 BCl3

```
            SOL  75-09-2 CH2Cl2
            CON  1 hour, -78 deg C

          STAGE(2)
            SOL  67-56-1 MeOH

        PRO  Q 391679-34-8

RX(15)  RCT  AX 96-33-3, Q 391679-34-8
        RGT  AY 121-44-8 Et3N
        PRO  AE 391679-42-8
        CAT  3375-31-3 Pd(OAc)2, 603-35-0 PPh3
        SOL  123-91-1 Dioxane
        CON  4 hours, 78 deg C
        NTE  stereoselective

RX(10)  RCT  AE 391679-42-8

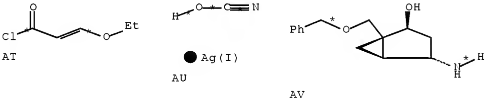
          STAGE(1)
            RGT  AG 1310-58-3 KOH
            SOL  7732-18-5 Water
            CON  overnight, room temperature

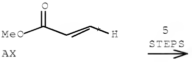
          STAGE(2)
            RGT  AH 7647-01-0 HCl
            SOL  7732-18-5 Water
            CON  room temperature, pH 2

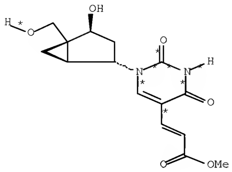
          STAGE(3)
            SOL  67-56-1 MeOH

        PRO  AF 391679-43-9


RX(62) OF 63 COMPOSED OF RX(14), RX(5), RX(6), RX(8), RX(15)
RX(62)   AT  +  AU  +  AV  +  AX  ===>  AE
```







AE
YIELD 48%

```
RX(14)    RCT  AT 6191-99-7, AU 3315-16-0

            STAGE(1)
               SOL  71-43-2 Benzene
               CON  SUBSTAGE(1) 2 hours, 100 deg C
                    SUBSTAGE(2) 45 minutes, reflux
                    SUBSTAGE(3) reflux -> room temperature

            STAGE(2)
               RCT  AV 191480-80-5
               SOL  68-12-2 DMF
               CON  SUBSTAGE(1) 0 deg C
                    SUBSTAGE(2) overnight, 0 deg C -> room temperature

          PRO  T 391679-36-0

RX(5)     RCT  T 391679-36-0

            STAGE(1)
               RGT  V 7664-93-9 H2SO4
               SOL  7732-18-5 Water, 64-17-5 EtOH
               CON  1 hour, reflux

            STAGE(2)
               RGT  D 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  neutralized

          PRO  U 391679-37-1

RX(6)     RCT  U 391679-37-1
          RGT  Y 7553-56-2 I2, Z 7697-37-2 HNO3
          PRO  X 391679-39-3
          SOL  7732-18-5 Water, 123-91-1 Dioxane
          CON  1 hour, 100 deg C
          NTE  regioselective

RX(8)     RCT  X 391679-39-3

            STAGE(1)
               RGT  R 10294-34-5 BCl3
```

```
            SOL  75-09-2 CH2Cl2
            CON  1 hour, -78 deg C

          STAGE(2)
            SOL  67-56-1 MeOH

         PRO  Q 391679-34-8

RX(15)   RCT  AX 96-33-3, Q 391679-34-8
         RGT  AY 121-44-8 Et3N
         PRO  AE 391679-42-8
         CAT  3375-31-3 Pd(OAc)2, 603-35-0 PPh3
         SOL  123-91-1 Dioxane
         CON  4 hours, 78 deg C
         NTE  stereoselective


L46  ANSWER 5 OF 24  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         138:271677  CASREACT  Full-text
TITLE:                    Process for the preparation of 1,5-diarylpyrazoles
                          useful as COX-2 inhibitors, including celecoxib, via
                          cyclocondensation of arylalkynones with arylhydrazines
INVENTOR(S):              Reddy, M. V. Ramana; Bell, Stanley C.
PATENT ASSIGNEE(S):       Onconova Therapeutics, Inc., USA
SOURCE:                   PCT Int. Appl., 25 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
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     WO 2003024958      A2   20030327      WO 2002-US29581   20020918
     WO 2003024958      A3   20031211
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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     US 20030109709     A1   20030612      US 2002-246565    20020918
     US 6906196         B2   20050614
     EP 1436285         A2   20040714      EP 2002-773451    20020918
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     NZ 532346          A    20051028      NZ 2002-532346    20020918
     IN 2004KN00496     A    20060818      IN 2004-KN496     20040415
     US 20050209459     A1   20050922      US 2005-118261    20050429
PRIORITY APPLN. INFO.:                     US 2001-323479P   20010918
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OTHER SOURCE(S):          MARPAT 138:271677
GI
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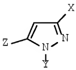
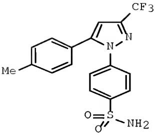


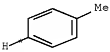
I



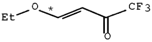
IV

AB Provided are processes for the preparation of diarylpyrazole derivs. I [wherein: X = trihalomethyl, C1-C6 alkyl, C6H3R1R2; R1, R2 = H, halo, OH, NO2, C1-C6 alkyl, C1-C6 alkoxy, CO2H, C1-C6 trihaloalkyl, cyano, alkylsulfonyl, sulfamyl, phosphonato, or hydroxyalkyl; Y, Z = (un)substituted (hetero)aryl]. Also provided are synthetic intermediates that are useful in the preparation of I. The processes involve cyclocondensation of arylalkynones ZC.tplbond.CCOX with arylhydrazines YNHNH2 or salts thereof. The claimed compds. include the above arylalkynones, and also a subset of I, the latter with X = CF3, Y = 4-H2NSO2C6H4, Z = (un)substituted 3-indolyl. Compds. I are well-known inhibitors of cyclooxygenase-2 (COX-2), and are useful for treatment of inflammation and related disorders, including arthritis (no data). The invention process uses readily available and inexpensive starting materials, and provides high yields of I with simplified isolation and purification steps. For example, alkenylation of toluene by EtOCH:CHCOCF3 and ZnCl2 in CH2Cl2 gives 4-MeC6H4CH:CHCOCF3, which is brominated (Br2 in CHCl3 at room temperature) and dehydrobrominated (KOH in refluxing EtOH) to give 4-MeC6H4C.tplbond.CCOCF3 (II). In a sep. reaction, sulfanilamide is diazotized (NaNO2, HCl) and reduced (SnCl2, HCl) to give 4-H2NSO2C6H4NHNH2 as the hydrochloride (III). Cyclization of II with III in refluxing EtOH over 4 h gives I [X = CF3, Y = 4-H2NSO2C6H4, Z = 4-MeC6H4], i.e., the drug celecoxib (IV). Similarly prepared was I [X = CH3, Y = 4-H2NSO2C6H4, Z = Ph].

RX(1) OF 15 A + B ===> C...

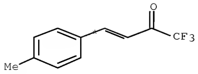


A



B

(1) $\longrightarrow$



C

RX(1) RCT A 108-88-3, B 17129-06-5
PRO C 232947-12-5
CAT 7646-85-7 ZnCl2
SOL 75-09-2 CH2Cl2
CON 3 hours, 22 deg C
NTE scalable

L46 ANSWER 6 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 138:271673 CASREACT Full-text
TITLE: Process for the preparation of 1,5-diarylpyrazoles useful as COX-2 inhibitors, including celecoxib, via cyclocondensation of phenylalkynones with phenylhydrazines
INVENTOR(S): Reddy, M. V. Ramana; Bell, Stanley C.
PATENT ASSIGNEE(S): Onconova Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024400	A2	20030327	WO 2002-US29566	20020918
WO 2003024400	A3	20030626		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2002330042	A1	20030401	AU 2002-330042	20020918
US 20030096853	A1	20030522	US 2002-245949	20020918
US 6579988	B2	20030617		
US 20030199707	A1	20031023	US 2003-423790	20030425
US 6706927	B2	20040316		

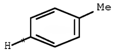
PRIORITY APPLN. INFO.: US 2001-323006P 20010918
US 2002-245949 20020918
WO 2002-US29566 20020918

OTHER SOURCE(S): MARPAT 138:271673
GI

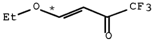
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Provided are processes for the preparation of diarylpyrazole derivs. I [wherein R1, R3 and R4 are independently selected from H, halogen, OH, NO2, lower alkyl, lower alkoxy, CO2H, C1-C6 trihaloalkyl, and cyano; and R2 is amino or lower alkyl]. Also provided are synthetic intermediates that are useful in the preparation of I. The processes involves cyclocondensation of phenylalkynones II with phenylhydrazines III or salts thereof. The claimed intermediates are the phenylalkynones II. Compds. I are well-known inhibitors of cyclooxygenase-2 (COX-2), and are useful for treatment of inflammation and related disorders, including arthritis (no data). The invention process uses readily available and inexpensive starting materials, and provides high yields of I with simplified isolation and purification steps. For example, alkenylation of toluene by EtOCH:CHCOCF3 and ZnCl2 in CH2Cl2 gives 4-MeC6H4CH:CHCOCF3, which is brominated (Br2 in CHCl3 at room temperature) and dehydrobrominated (KOH in refluxing EtOH) to give 4-MeC6H4C.tplbond.CCOCF3 (IV). In a sep. reaction, sulfanilamide is diazotized (NaNO2, HCl) and reduced (SnCl2, HCl) to give 4-H2NSO2C6H4NHNH2 as the hydrochloride (V). Cyclization of IV with V in refluxing EtOH over 4 h gives I [R1 = 4-Me, R2 = NH2, R3 = R4 = H], i.e., the drug celecoxib.

RX(1) OF 13 A + B ===> C...

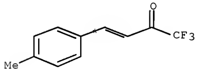


A



B

(1) →

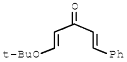


C

RX(1) RCT A 108-88-3, B 17129-06-5
PRO C 232947-12-5
CAT 7646-85-7 ZnCl2
SOL 75-09-2 CH2Cl2
CON 3 hours, 22 deg C
NTE scalable

L46 ANSWER 7 OF 24 CASREACT

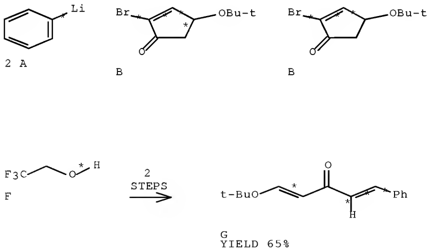
ACCESSION NUMBER: 138:89482 CASREACT Full-text
TITLE: The Retro-Nazarov Reaction
AUTHOR(S): Harmata, Michael; Lee, Dong Reyoul
CORPORATE SOURCE: Department of Chemistry, University of Missouri-Columbia, Columbia, MO, 65211, USA
SOURCE: Journal of the American Chemical Society (2002), 124(48), 14328-14329
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

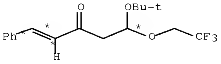


I

AB Treatment of 2-bromo-4-t-butoxy-2-cyclopentenone with an amine base in refluxing trifluoroethanol afforded a ring-opened product in moderate yield. The mechanism of the reaction has been formulated as a retro-Nazarov reaction in which an oxyallylic cation undergoes ring-opening to a dienone. Several other examples of the reaction have been established through a protocol involving the conjugate addition of an organocuprate to 2-bromo-4-t-butoxy-2-cyclopentenone followed by treatment of the adducts with base in refluxing trifluoroethanol to provided divinyl ketones, e.g., I.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(22) OF 31 COMPOSED OF RX(1), RX(2)
RX(22) 2 A + 2 B + F ===> G + H





H
YIELD 9%

```
RX(1)      RCT  A 591-51-5

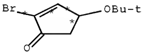
             STAGE(1)
                RGT  D 7681-65-4 CuI
                SOL  60-29-7 Et2O
                CON  SUBSTAGE(1) room temperature -> -78 deg C
                     SUBSTAGE(2) 15 minutes, -78 deg C
                     SUBSTAGE(3) 15 minutes, 0 deg C
                     SUBSTAGE(4) 15 minutes, room temperature

             STAGE(2)
                RCT  B 485401-53-4
                SOL  60-29-7 Et2O
                CON  SUBSTAGE(1) 10 minutes, -78 deg C
                     SUBSTAGE(2) 15 minutes, -78 deg C
                     SUBSTAGE(3) 10 minutes, 0 deg C
                     SUBSTAGE(4) 10 minutes, room temperature

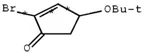
           PRO  C 485401-54-5

RX(2)      RCT  C 485401-54-5, F 75-89-8
           RGT  I 121-44-8 Et3N
           PRO  G 485401-55-6, H 485401-66-9
           SOL  75-89-8 F3CCH2OH
           CON  1 hour, reflux
           NTE  optimization study, retro-Nazarov reaction, stereoselective


RX(23) OF 31 COMPOSED OF RX(3), RX(13)
RX(23)     2 B  +  2 J  +  F  ===>  AH  +  AI
```



B



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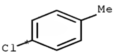
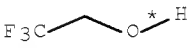
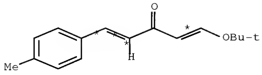


2 J

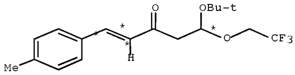


F

2
STEPS
→



AH
YIELD 52%



AI
YIELD 9%

```
RX(3)      RCT  B 485401-53-4

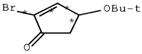
             STAGE(1)
                RGT  D 7681-65-4 CuI
                SOL  60-29-7 Et2O
                CON  SUBSTAGE(1) room temperature -> -78 deg C
                     SUBSTAGE(2) 15 minutes, -78 deg C
                     SUBSTAGE(3) 15 minutes, 0 deg C
                     SUBSTAGE(4) 15 minutes, room temperature

             STAGE(2)
                RCT  J 106-43-4
                SOL  60-29-7 Et2O
                CON  SUBSTAGE(1) 10 minutes, -78 deg C
                     SUBSTAGE(2) 15 minutes, -78 deg C
                     SUBSTAGE(3) 10 minutes, 0 deg C
                     SUBSTAGE(4) 10 minutes, room temperature

           PRO  K 485401-56-7

RX(13)     RCT  K 485401-56-7, F 75-89-8
           RGT  I 121-44-8 Et3N
           PRO  AH 485401-67-0, AI 485401-68-1
           SOL  75-89-8 F3CCH2OH
           CON  1 hour, reflux
           NTE  retro-Nazarov reaction, stereoselective


RX(24) OF 31 COMPOSED OF RX(4), RX(14)
RX(24)     2 B  +  2 L  +  F  ===>  AJ  +  AK
```



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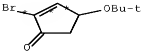

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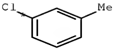
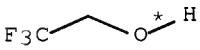
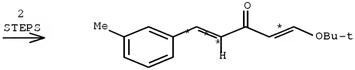


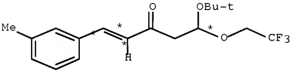
2 L



F



AJ
YIELD 59%



AK
YIELD 10%

```
RX(4)     RCT  B 485401-53-4

            STAGE(1)
               RGT  D 7681-65-4 CuI
               SOL  60-29-7 Et2O
               CON  SUBSTAGE(1) room temperature -> -78 deg C
                    SUBSTAGE(2) 15 minutes, -78 deg C
                    SUBSTAGE(3) 15 minutes, 0 deg C
                    SUBSTAGE(4) 15 minutes, room temperature

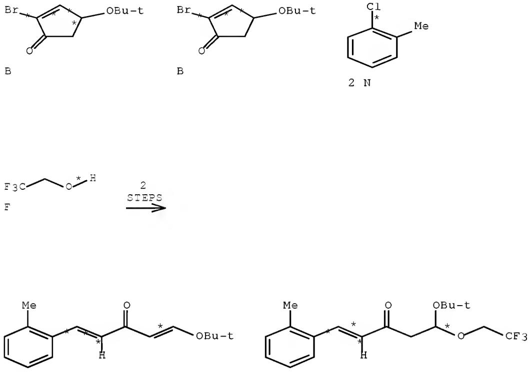
            STAGE(2)
               RCT  L 108-41-8
               SOL  60-29-7 Et2O
               CON  SUBSTAGE(1) 10 minutes, -78 deg C
                    SUBSTAGE(2) 15 minutes, -78 deg C
                    SUBSTAGE(3) 10 minutes, 0 deg C
                    SUBSTAGE(4) 10 minutes, room temperature

          PRO  M 485401-57-8

RX(14)    RCT  M 485401-57-8, F 75-89-8
          RGT  I 121-44-8 Et3N
          PRO  AJ 485401-69-2, AK 485401-77-2
          SOL  75-89-8 F3CCH2OH
```

CON 1 hour, reflux
NTE retro-Nazarov reaction, stereoselective

RX(25) OF 31 COMPOSED OF RX(5), RX(15)
RX(25) 2 B + 2 N + F ===> AL + AM



AL
YIELD 60%

AM
YIELD 10%

RX(5) RCT B 485401-53-4

STAGE(1)
RGT D 7681-65-4 CuI
SOL 60-29-7 Et2O
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 15 minutes, -78 deg C
SUBSTAGE(3) 15 minutes, 0 deg C
SUBSTAGE(4) 15 minutes, room temperature

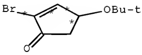
STAGE(2)
RCT N 95-49-8
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 10 minutes, -78 deg C
SUBSTAGE(2) 15 minutes, -78 deg C
SUBSTAGE(3) 10 minutes, 0 deg C
SUBSTAGE(4) 10 minutes, room temperature

PRO O 485401-58-9

RX(15) RCT O 485401-58-9, F 75-89-8

RGT I 121-44-8 Et3N
PRO AL 485401-70-5, AM 485401-78-3
SOL 75-89-8 F3CCH2OH
CON 1 hour, reflux
NTE retro-Nazarov reaction, stereoselective

RX(26) OF 31 COMPOSED OF RX(6), RX(16)
RX(26) 2 B + 2 P + F ===> AN + AO



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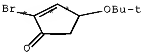

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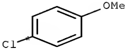
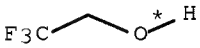


2 P



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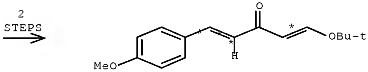
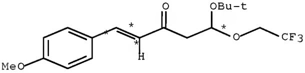


AN
YIELD 59%



AO
YIELD 8%

RX(6) RCT B 485401-53-4

STAGE(1)
RGT D 7681-65-4 CuI
SOL 60-29-7 Et2O
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 15 minutes, -78 deg C
SUBSTAGE(3) 15 minutes, 0 deg C
SUBSTAGE(4) 15 minutes, room temperature

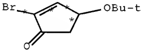
STAGE(2)
RCT P 623-12-1
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 10 minutes, -78 deg C

```
                    SUBSTAGE(2) 15 minutes, -78 deg C
                    SUBSTAGE(3) 10 minutes, 0 deg C
                    SUBSTAGE(4) 10 minutes, room temperature

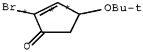
          PRO  Q 485401-59-0

RX(16)    RCT  Q 485401-59-0, F 75-89-8
          RGT  I 121-44-8 Et3N
          PRO  AN 485401-71-6, AO 485401-79-4
          SOL  75-89-8 F3CCH2OH
          CON  1 hour, reflux
          NTE  retro-Nazarov reaction, stereoselective


RX(27) OF 31 COMPOSED OF RX(7), RX(17)
RX(27)    2 B  +  2 R  +  F  ===>  AP  +  AQ
```



B



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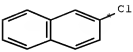
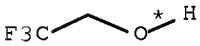


2 R



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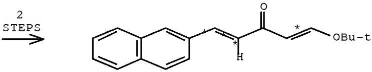
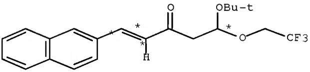


AP
YIELD 65%



AQ
YIELD 8%

```
RX(7)     RCT  B 485401-53-4

            STAGE(1)
               RGT  D 7681-65-4 CuI
               SOL  60-29-7 Et2O
               CON  SUBSTAGE(1) room temperature -> -78 deg C
                    SUBSTAGE(2) 15 minutes, -78 deg C
```

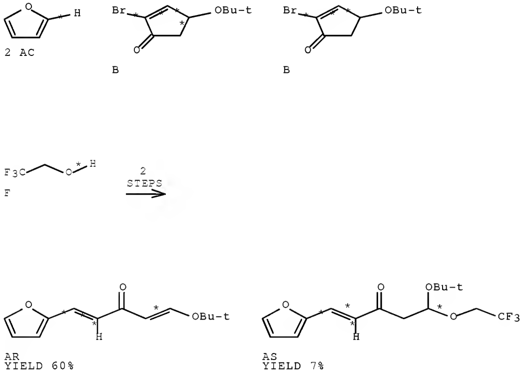
```
                SUBSTAGE(3) 15 minutes, 0 deg C
                SUBSTAGE(4) 15 minutes, room temperature

        STAGE(2)
           RCT  R 91-58-7
           SOL  60-29-7 Et2O
           CON  SUBSTAGE(1) 10 minutes, -78 deg C
                SUBSTAGE(2) 15 minutes, -78 deg C
                SUBSTAGE(3) 10 minutes, 0 deg C
                SUBSTAGE(4) 10 minutes, room temperature

      PRO  S 485401-60-3

RX(17)    RCT  S 485401-60-3, F 75-89-8
          RGT  I 121-44-8 Et3N
          PRO  AP 485401-72-7, AQ 485401-80-7
          SOL  75-89-8 F3CCH2OH
          CON  1 hour, reflux
          NTE  retro-Nazarov reaction, stereoselective


RX(31) OF 31 COMPOSED OF RX(11), RX(18)
RX(31)    2 AC  +  2 B  +  F  ===>  AR  +  AS
```




```
RX(11)    RCT  AC 110-00-9

        STAGE(1)
           RGT  AE 109-72-8 BuLi
           SOL  109-99-9 THF
           CON  SUBSTAGE(1) -78 deg C
```

```
                    SUBSTAGE(2) 24 hours, room temperature

            STAGE(2)
               RGT  D 7681-65-4 CuI
               SOL  60-29-7 Et2O
               CON  SUBSTAGE(1) 10 minutes, -78 deg C
                    SUBSTAGE(2) 15 hours, 0 deg C
                    SUBSTAGE(3) 15 hours, room temperature

            STAGE(3)
               RCT  B 485401-53-4
               CON  SUBSTAGE(1) 15 minutes, -78 deg C
                    SUBSTAGE(2) 10 minutes, 0 deg C
                    SUBSTAGE(3) 15 hours, room temperature

          PRO  AD 485401-64-7

RX(18)    RCT  AD 485401-64-7, F 75-89-8
          RGT  I 121-44-8 Et3N
          PRO  AR 485401-73-8, AS 485401-81-8
          SOL  75-89-8 F3CCH2OH
          CON  1 hour, reflux
          NTE  retro-Nazarov reaction, stereoselective
```

L46 ANSWER 8 OF 24 CASREACT

ACCESSION NUMBER: 136:87214 CASREACT Full-text

TITLE: A 3-hydroxychromone with dramatically improved fluorescence properties

AUTHOR(S): Klymchenko, Andrey S.; Ozturk, Turan; Pivovarenko, Vasyl G.; Demchenko, Alexander P.

CORPORATE SOURCE: TUBITAK Marmara Research Center, Gebze-Kocaeli, 41470, Turk.

SOURCE: Tetrahedron Letters (2001), 42(45), 7967-7970
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

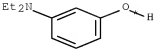
DOCUMENT TYPE: Journal

LANGUAGE: English

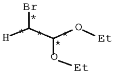
AB A new 3-hydroxychromone derivative, 2-[6-(diethylamino)benzo[b]furan-2-yl]-3-hydroxychromone, has been synthesized by a concise route. Possessing dual emission common for 3-hydroxyflavones, it exhibits strong red shifts of both absorption and fluorescence spectra, which makes it the longest wavelength fluorescent dye among all known chromones. It also demonstrates a significant increase in fluorescence quantum yield in aprotic solvents and shift in solvent-polarity-dependent switch between normal and tautomer emissive forms. This derivative offers new possibilities in designing novel mol. sensors.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
RX(8) OF 10 COMPOSED OF RX(1), RX(2), RX(3)
RX(8)     A  +  B  +  F  +  J  ===>  K
```



A



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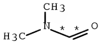

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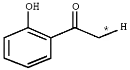
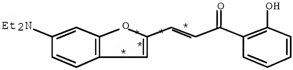


J

3
STEPS



K

```
RX(1)       RCT  A 91-68-9

              STAGE(1)
                 RGT   D 7646-69-7 NaH
                 SOL   68-12-2 DMF

              STAGE(2)
                 RCT   B 2032-35-1
                 CAT   7681-11-0 KI
                 SOL   67-68-5 DMSO

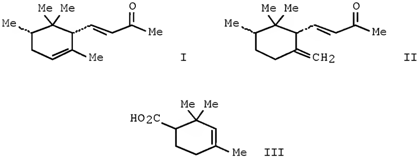
            PRO  C 108639-47-0

RX(2)       RCT  C 108639-47-0, F 68-12-2
            RGT  I 10025-87-3 POCl3
            PRO  H 126174-13-8
            SOL  68-12-2 DMF

RX(3)       RCT  H 126174-13-8, J 118-93-4
            RGT  L 1310-58-3 KOH
            PRO  K 386736-83-0
            SOL  64-17-5 EtOH, 7732-18-5 Water
```

L46 ANSWER 9 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 134:178683 CASREACT Full-text
TITLE: Synthesis of both enantiomers of cis-α-irone and cis-γ-irone, principal constituents of iris oil, via resolution of (±)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid
AUTHOR(S): Inoue, T.; Kiyota, H.; Oritani, T.
CORPORATE SOURCE: Department of Applied Bioorganic Chemistry, Division of Life Science, Graduate School of Agricultural Science, Tohoku University, Sendai, Aoba-ku, 981-8555, Japan
SOURCE: Tetrahedron: Asymmetry (2000), 11(18), 3807-3818
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



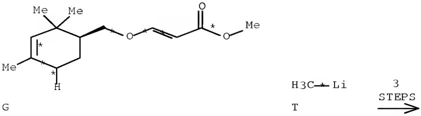
I

II

III

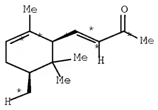
AB The principal constituents of iris oil, (-)-cis-α-irone (I) and (-)-cis-γ-irone (II), and their enantiomers, were synthesized from (-)- and (+)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acids (III). The racemic acid was resolved by recrystn. of its salt with a chiral amine, or by enzymic hydrolysis of the corresponding alc. The fragrances of (-)-(1R,5S)-cis-α-irone and (-)-(1R,5S)-cis-γ-irone were superior to those of (+)-(1S,5R)-cis-α-irone and (+)-(1S,5R)-cis-γ-irone.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(29) OF 56 COMPOSED OF RX(4), RX(5), RX(7)
RX(29) G + T ===> U



G

T



U
YIELD 68%

RX(4)   RCT G 326907-23-7
         RGT K 75-75-2 MeSO3H
         PRO J 326907-24-8
         SOL 60-29-7 Et2O
         NTE stereoselective

RX(5)   RCT J 326907-24-8
         RGT M 1310-73-2 NaOH
         PRO L 326907-25-9
         SOL 67-56-1 MeOH
         NTE stereoselective

RX(7)   RCT L 326907-25-9

STAGE(1)
RGT V 4111-54-0 LiN(Pr-i)2
SOL 109-99-9 THF

STAGE(2)
RGT W 124-63-0 MeSO2Cl, X 110-86-1 Pyridine
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT Q 7440-66-6 Zn, Y 7681-82-5 NaI
SOL 110-71-4 (CH2OMe)2

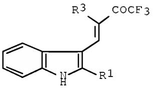
STAGE(4)
RCT T 917-54-4
SOL 60-29-7 Et2O

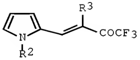
PRO U 89888-03-9
NTE stereoselective

L46 ANSWER 10 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 132:93182 CASREACT Full-text
TITLE: Synthesis of indolyl- and pyrrolyl-substituted trifluoromethyl-containing enones
AUTHOR(S): Sanin, A. V.; Nenaidenko, V. G.; Balenkova, E. S.
CORPORATE SOURCE: Faculty of Chemistry, Moscow State University, Moscow, 119899, Russia

SOURCE: Russian Journal of Organic Chemistry (Translation of Zhurnal Organicheskoi Khimii) (1999), 35(5), 711-714
CODEN: RJOCEQ; ISSN: 1070-4280
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

GI

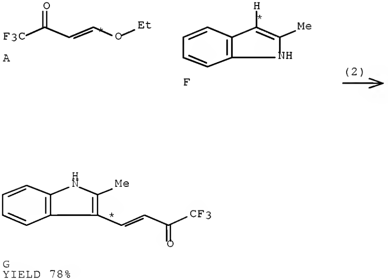

II


III

AB Indoles and pyrroles react with (E)-4-ethoxy-1,1,1-trifluoro-3-buten-2-one (I) and 3-(ethoxymethylene)-1,1,1,5,5,5-hexafluoro-2,4-pentanedione in the presence of ZnCl2 to give hetaryl-substituted enones II (R1 = Me, Ph; R3 = H, COCF3) and III (R2 = H, Me; R3 = H, COCF3) containing, resp., one or two trifluoroacetyl groups. The reactions with I are stereospecific, and only E isomers of the corresponding enones are formed.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 9 A + F ===> G

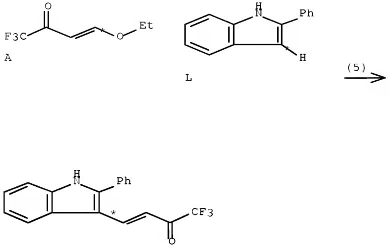


G
YIELD 78%

RX(2) RCT A 59938-06-6, F 95-20-5
RGT H 7646-85-7 ZnCl2
PRO G 202074-31-5

SOL 75-09-2 CH2Cl2

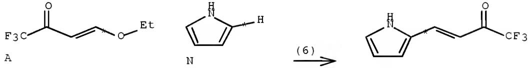
RX(5) OF 9 A + L ===> M



M
YIELD 56%

RX(5) RCT A 59938-06-6, L 948-65-2
RGT H 7646-85-7 ZnCl2
PRO M 202074-32-6
SOL 75-09-2 CH2Cl2

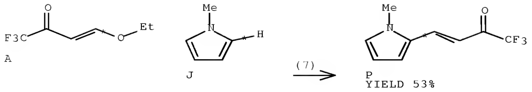
RX(6) OF 9 A + N ===> O



O
YIELD 37%

RX(6) RCT A 59938-06-6, N 109-97-7
RGT H 7646-85-7 ZnCl2
PRO O 202074-27-9
SOL 75-09-2 CH2Cl2

RX(7) OF 9 A + J ===> P



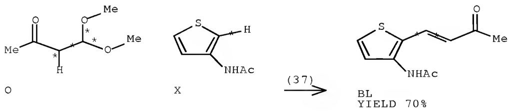
RX(7) RCT A 59938-06-6, J 96-54-8
RGT H 7646-85-7 ZnCl2
PRO P 202074-28-0
SOL 75-09-2 CH2Cl2

L46 ANSWER 11 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 129:216528 CASREACT Full-text
TITLE: α-Vinylation of β-aminothiophene derivatives. synthesis of 6-functionalized thieno[3,2-b]pyridines
AUTHOR(S): Berkaoui, M'hamed; Outurquin, Francis; Paulmier, Claude
CORPORATE SOURCE: Laboratoire de Synthese Thio et Selenoorganique, Universite de Rouen, Mont-Saint-Aignan, F-7682 I1, Fr.
SOURCE: Tetrahedron (1998), 54(31), 9055-9066
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The acid-catalyzed reductive α-alkylation of β-aminothiophene derivs. was applied to the N-(3-thienyl)acetamide and alkyl N-(3-thienyl)carbamates. Without reduction, β-amino α- vinylthiophenes were obtained when α-branched aldehydes were used. β-(3-Amino-2-thienyl)α,β-unsatd. ketones, esters and nitriles were also prepared from the corresponding α-functionalized acetals. These amines are intermediates in the formation of thieno[3,2-b]pyridines bearing a functional group at the β-position of the pyridine ring.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(37) OF 56 O + X ===> BL



RX(37) RCT O 5436-21-5, X 42602-67-5

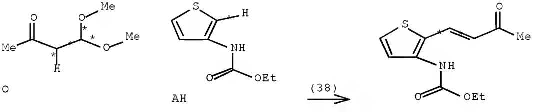
```
          STAGE(1)
             SOL   75-09-2 CH2Cl2

          STAGE(2)
             RGT   D 7647-01-0 HCl

          STAGE(3)
             RGT   E 1310-73-2 NaOH

       PRO   BL 75877-30-4
```

RX(38) OF 56   O + AH ===> BM



O

AH

(38)

BM
YIELD 67%

```
RX(38)    RCT   O 5436-21-5, AH 701-93-9

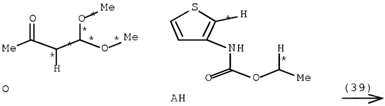
          STAGE(1)
             SOL   75-09-2 CH2Cl2

          STAGE(2)
             RGT   D 7647-01-0 HCl

          STAGE(3)
             RGT   E 1310-73-2 NaOH

       PRO   BM 212570-81-5
```

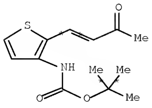
RX(39) OF 56   O + AH ===> BA...



O

AH

(39)



BA
YIELD 80%

RX(39)   RCT O 5436-21-5, AH 701-93-9

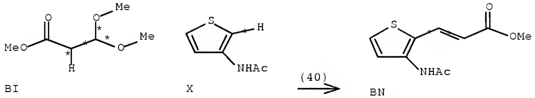
  STAGE(1)
    SOL 75-09-2 CH2Cl2

  STAGE(2)
    RGT D 7647-01-0 HCl

  STAGE(3)
    RGT E 1310-73-2 NaOH

 PRO BA 212570-83-7

RX(40) OF 56   BI + X ===> BN



BI   X   BN
YIELD 88%

RX(40)   RCT BI 7424-91-1, X 42602-67-5

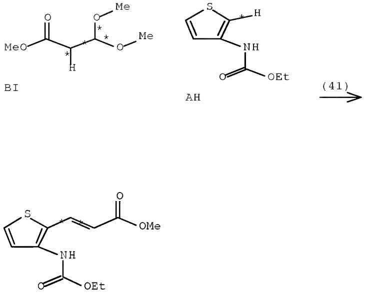
  STAGE(1)
    SOL 75-09-2 CH2Cl2

  STAGE(2)
    RGT D 7647-01-0 HCl

  STAGE(3)
    RGT E 1310-73-2 NaOH

 PRO BN 75877-28-0

RX(41) OF 56   BI + AH ===> BO



BO
YIELD 85%

RX(41) RCT BI 7424-91-1, AH 701-93-9

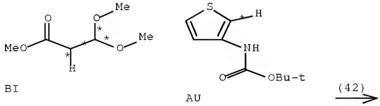
STAGE(1)
SOL 75-09-2 CH2Cl2

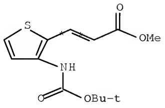
STAGE(2)
RGT D 7647-01-0 HCl

STAGE(3)
RGT E 1310-73-2 NaOH

PRO BO 212571-14-7

RX(42) OF 56 BI + AU ===> BE...





BE
YIELD 75%

RX(42) RCT BI 7424-91-1, AU 19228-91-2

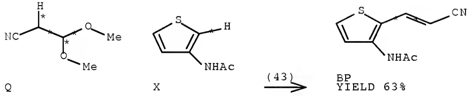
STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT D 7647-01-0 HCl

STAGE(3)
RGT E 1310-73-2 NaOH

PRO BE 212570-86-0

RX(43) OF 56 Q + X ===> BP



Q X BP
YIELD 63%

RX(43) RCT Q 57597-62-3, X 42602-67-5

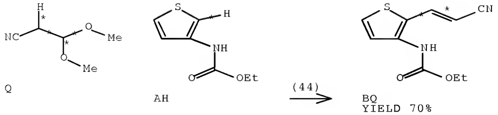
STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT D 7647-01-0 HCl

STAGE(3)
RGT E 1310-73-2 NaOH

PRO BP 212570-88-2

RX(44) OF 56 Q + AH ===> BQ



RX(44)   RCT Q 57597-62-3, AH 701-93-9

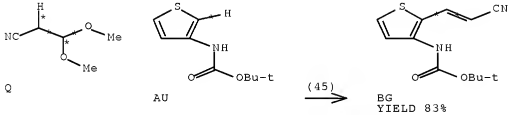
    STAGE(1)
        SOL 75-09-2 CH2Cl2

    STAGE(2)
        RGT D 7647-01-0 HCl

    STAGE(3)
        RGT E 1310-73-2 NaOH

    PRO BQ 212570-90-6

RX(45) OF 56   Q + AU ===> BG...



RX(45)   RCT Q 57597-62-3, AU 19228-91-2

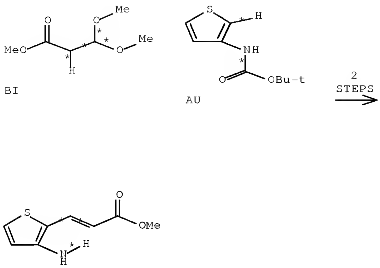
    STAGE(1)
        SOL 75-09-2 CH2Cl2

    STAGE(2)
        RGT D 7647-01-0 HCl

    STAGE(3)
        RGT E 1310-73-2 NaOH

    PRO BG 212570-92-8

RX(51) OF 56 COMPOSED OF RX(42), RX(31)
RX(51)   BI + AU ===> BF



BF
YIELD 55%

RX(42)   RCT   BI 7424-91-1, AU 19228-91-2

  STAGE(1)
    SOL   75-09-2 CH2Cl2

  STAGE(2)
    RGT   D 7647-01-0 HCl

  STAGE(3)
    RGT   E 1310-73-2 NaOH

PRO   BE 212570-86-0

RX(31)   RCT   BE 212570-86-0

  STAGE(1)
    RGT   BC 10035-10-6 HBr, BD 64-19-7 AcOH

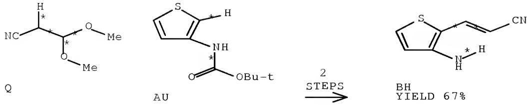
  STAGE(2)
    SOL   60-29-7 Et2O

  STAGE(3)
    SOL   7732-18-5 Water

  STAGE(4)
    RGT   E 1310-73-2 NaOH

PRO   BF 75877-27-9

RX(52) OF 56 COMPOSED OF RX(45), RX(32)
RX(52)   Q + AU ===> BH



RX(45) RCT Q 57597-62-3, AU 19228-91-2

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT D 7647-01-0 HCl

STAGE(3)
RGT E 1310-73-2 NaOH

PRO BG 212570-92-8

RX(32) RCT BG 212570-92-8

STAGE(1)
RGT BC 10035-10-6 HBr, BD 64-19-7 AcOH

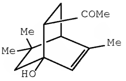
STAGE(2)
RGT BB 60-29-7 Et2O

STAGE(3)
SOL 7732-18-5 Water

STAGE(4)
RGT E 1310-73-2 NaOH

PRO BH 212570-96-2

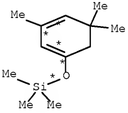
L46 ANSWER 12 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 125:329061 CASREACT Full-text
TITLE: Reactions of endocyclic linearly conjugated dienolates with Michael acceptors leading to bicyclo[2.2.2]octane derivatives. Application to the synthesis of C13 degradation products of carotenoids
AUTHOR(S): Ito, Nobuhiko; Etoh, Takeaki
CORPORATE SOURCE: Research Development Lab., Soda Aromatic Co., Ltd., Noda, 270-02, Japan
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1996), (19), 2397-2405
CODEN: JCPRB4; ISSN: 0300-922X
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



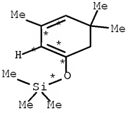
I

AB The endocyclic linearly conjugated dienolates from substituted cyclohex-2-enones react with but-3-en-2-one, substituted Me propenoates, but-3-yn-2-one and Me propiolate to afford bicyclo[2.2.2]oct-2-en-1-ols, e.g. I, and bicyclo[2.2.2]octa-2,5-dien-1-ols. The AlCl3-catalyzed reaction of 3,5,5-trimethyl-1-(trimethylsiloxy)cyclohexa-1,3-diene with (E)-4-acetoxy- and (E)-4-methoxybut-3-en-2-one provides trans-8-acetoxy-7-acetyl-3,5,5-trimethyl-1-(trimethylsiloxy)bicyclo[2.2.2] oct-2-enes and trans-7-acetyl-8-methoxy-3,5,5-trimethyl-1- (trimethylsiloxy)bicyclo[2.2.2]oct-2-enes. Starting from these bicyclo[2.2.2]octenes, the C13 degradation products of carotenoids including 3-oxo-a-ionone, blumenol-C and 1,3,7,7-tetramethyl-2- oxabicyclo[4.4.0]decan-9-one have been synthesized.

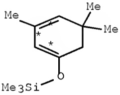
RX(2) OF 4 4 G + 4 H ===> I + J + K + L



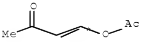
G



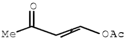
G



2 G

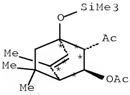


2 H

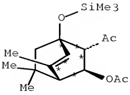


2 H

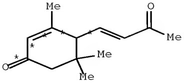
(2) →



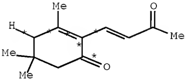
I
YIELD 13%



J
YIELD 15%



K
YIELD 30%



L
YIELD 10%

RX(2)   RCT G 80699-65-6, H 51731-15-8
         RGT M 7446-70-0 AlCl3
         PRO I 141915-26-6, J 141979-75-1, K 79734-43-3, L 183282-14-6
         SOL 75-09-2 CH2Cl2

L46 ANSWER 13 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 121:133898 CASREACT Full-text

TITLE: Synthesis of heterocyclic compounds with hydroxymethylene ketones. XIV. Contribution to the regioselectivity of the reaction of acetoacetaldehyde with tryptamine

AUTHOR(S): Teuber, Hans-Joachim; Quintanilla-Licea, Ramiro

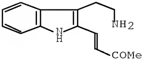
CORPORATE SOURCE: Inst. fuer Organische Chemie, J.W. Goethe-Univ., Frankfurt/Main, Germany

SOURCE: Journal fuer Praktische Chemie/Chemiker-Zeitung (1994), 336(5), 452-7
CODEN: JPCCEM; ISSN: 0941-1216

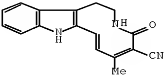
DOCUMENT TYPE: Journal

LANGUAGE: German

GI



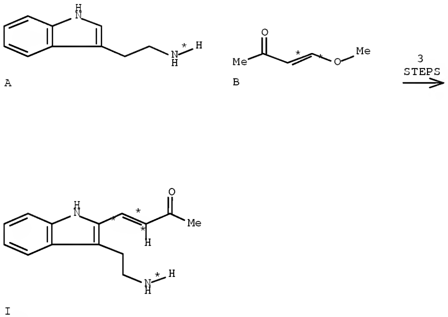
I



II

AB The range of substitution products of tryptamine with acetoacetaldehyde as substituent at the basic or the indole nitrogen is completed by a product I containing the substituent in the indole α-position. I is formed by ring opening of 1,2,3,4-tetrahydro-1-(2-oxopropyl)-β-carboline. The synthesis of the azocinoindole II is described. Reaction conditions are described and the 1H-NMR spectra comparatively discussed.

RX(10) OF 13 COMPOSED OF RX(1), RX(2), RX(3)
RX(10) A + B ===> I



YIELD 41%

```
RX(1)     RCT  A 61-54-1, B 4652-27-1
          PRO  C 157103-24-7
          SOL  75-09-2 CH2Cl2

RX(2)     RCT  C 157103-24-7
          RGT  F 7647-01-0 HCl
          PRO  E 157103-26-9
          SOL  7732-18-5 Water, 67-56-1 MeOH

RX(3)     RCT  E 157103-26-9
          PRO  I 157103-27-0
          SOL  7732-18-5 Water, 67-56-1 MeOH
          NTE  thermal
```

L46 ANSWER 14 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 118:39323 CASREACT Full-text

TITLE: Synthesis of carbocyclic nucleosides: synthesis of (±)-2,2-bis(hydroxymethyl)cyclopropyl nucleosides

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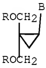
GI

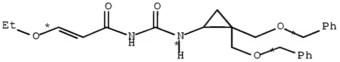


I

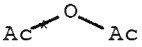
AB Treatment of cyclopropanecarboxylic acid I (R = CH2Ph, B = CO2H) with Et chloroformate and NaN3 followed by thermolysis of the resulting keto azide I (B = CON3) at 80° provided the corresponding isocyanate I (B = NCO), which was then converted into I (B = NH2, NHCONH2) (II). The racemic 2,2-bis(hydroxymethyl)cyclopropylpyrimidine nucleosides, e.g. I (R = H, B = adenine, guanine, thymine, uracil), were prepared from II. None of the carbocyclic nucleosides showed any significant anti-HIV activity.

RX(155) OF 201 COMPOSED OF RX(9), RX(10), RX(11), RX(13), RX(15), RX(16)

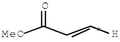
RX(155) S + 2 V + AF ===> AG



S

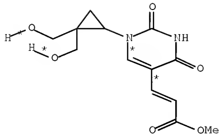


2 V



AF

6
STEPS
→



AG

```
RX(9)       RCT   S 135345-90-3
            RGT   M 7664-41-7 NH3
            PRO   T 135345-91-4

RX(10)      RCT   T 135345-91-4
            PRO   U 135345-83-4
            NTE   H2/PD

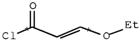
RX(11)      RCT   U 135345-83-4, V 108-24-7
            PRO   W 145215-09-4

RX(13)      RCT   W 145215-09-4
            RGT   AA 10377-51-2 LiI
            PRO   Z 145215-11-8
            NTE   (NH4)2[CE(NO3)6]

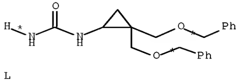
RX(15)      RCT   Z 145215-11-8
            RGT   AC 124-41-4 NaOMe
            PRO   AE 145215-14-1
            SOL   67-56-1 MeOH

RX(16)      RCT   AF 96-33-3, AE 145215-14-1
            RGT   AH 603-35-0 PPh3
            PRO   AG 145215-18-5
            CAT   3375-31-3 Pd(OAc)2

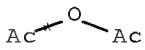
RX(157) OF 201 COMPOSED OF RX(8), RX(9), RX(10), RX(11), RX(13), RX(15), RX(16)
RX(157)    R  +  L  +  2 V  +  AF  ===>  AG
```



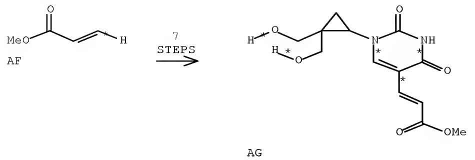
R



L



2 V




```
RX(8)      RCT  R 99471-66-6, L 135345-89-0
           PRO  S 135345-90-3

RX(9)      RCT  S 135345-90-3
           RGT  M 7664-41-7 NH3
           PRO  T 135345-91-4

RX(10)     RCT  T 135345-91-4
           PRO  U 135345-83-4
           NTE  H2/PD

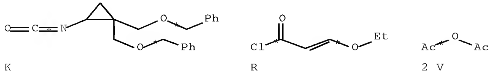
RX(11)     RCT  U 135345-83-4, V 108-24-7
           PRO  W 145215-09-4

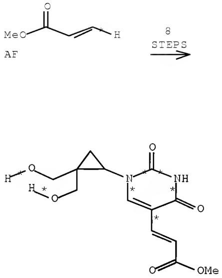
RX(13)     RCT  W 145215-09-4
           RGT  AA 10377-51-2 LiI
           PRO  Z 145215-11-8
           NTE  (NH4)2[CE(NO3)6]

RX(15)     RCT  Z 145215-11-8
           RGT  AC 124-41-4 NaOMe
           PRO  AE 145215-14-1
           SOL  67-56-1 MeOH

RX(16)     RCT  AF 96-33-3, AE 145215-14-1
           RGT  AH 603-35-0 PPh3
           PRO  AG 145215-18-5
           CAT  3375-31-3 Pd(OAc)2


RX(159) OF 201 COMPOSED OF RX(5), RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),
           RX(16)
RX(159)    K  +  R  +  2 V  +  AF  ===>  AG
```





AF

AG

```
RX(5)       RCT  K 135345-85-6
            RGT  M 7664-41-7 NH3
            PRO  L 135345-89-0

RX(8)       RCT  R 99471-66-6, L 135345-89-0
            PRO  S 135345-90-3

RX(9)       RCT  S 135345-90-3
            RGT  M 7664-41-7 NH3
            PRO  T 135345-91-4

RX(10)      RCT  T 135345-91-4
            PRO  U 135345-83-4
            NTE  H2/PD

RX(11)      RCT  U 135345-83-4, V 108-24-7
            PRO  W 145215-09-4

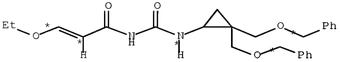
RX(13)      RCT  W 145215-09-4
            RGT  AA 10377-51-2 LiI
            PRO  Z 145215-11-8
            NTE  (NH4)2[CE(NO3)6]

RX(15)      RCT  Z 145215-11-8
            RGT  AC 124-41-4 NaOMe
            PRO  AE 145215-14-1
            SOL  67-56-1 MeOH

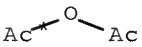
RX(16)      RCT  AF 96-33-3, AE 145215-14-1
            RGT  AH 603-35-0 PPh3
            PRO  AG 145215-18-5
            CAT  3375-31-3 Pd(OAc)2
```

RX(165) OF 201 COMPOSED OF RX(9), RX(10), RX(11), RX(13), RX(15), RX(16),
RX(17)

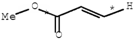
RX(165) S + 2 V + AF ===> AJ



S

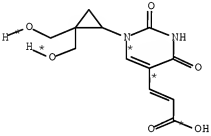


2 V



AF

7
STEPS
→



AJ

```
RX(9)     RCT  S 135345-90-3
          RGT  M 7664-41-7 NH3
          PRO  T 135345-91-4

RX(10)    RCT  T 135345-91-4
          PRO  U 135345-83-4
          NTE  H2/PD

RX(11)    RCT  U 135345-83-4, V 108-24-7
          PRO  W 145215-09-4

RX(13)    RCT  W 145215-09-4
          RGT  AA 10377-51-2 LiI
          PRO  Z 145215-11-8
          NTE  (NH4)2[CE(NO3)6]

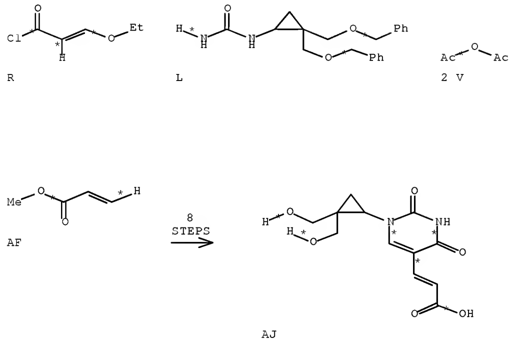
RX(15)    RCT  Z 145215-11-8
          RGT  AC 124-41-4 NaOMe
          PRO  AE 145215-14-1
```

```
          SOL   67-56-1 MeOH

RX(16)    RCT   AF 96-33-3, AE 145215-14-1
          RGT   AH 603-35-0 PPh3
          PRO   AG 145215-18-5
          CAT   3375-31-3 Pd(OAc)2

RX(17)    RCT   AG 145215-18-5
          RGT   AK 1310-73-2 NaOH
          PRO   AJ 145215-19-6


RX(167) OF 201 COMPOSED OF RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),
          RX(16), RX(17)
RX(167)   R  +  L  +  2 V  +  AF  ===>  AJ
```




```
RX(8)     RCT   R 99471-66-6, L 135345-89-0
          PRO   S 135345-90-3

RX(9)     RCT   S 135345-90-3
          RGT   M 7664-41-7 NH3
          PRO   T 135345-91-4

RX(10)    RCT   T 135345-91-4
          PRO   U 135345-83-4
          NTE   H2/PD

RX(11)    RCT   U 135345-83-4, V 108-24-7
          PRO   W 145215-09-4

RX(13)    RCT   W 145215-09-4
          RGT   AA 10377-51-2 LiI
```

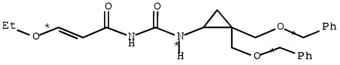
```
          PRO  Z 145215-11-8
          NTE  (NH4)2[CE(NO3)6]

RX(15)    RCT  Z 145215-11-8
          RGT  AC 124-41-4 NaOMe
          PRO  AE 145215-14-1
          SOL  67-56-1 MeOH

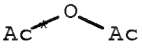
RX(16)    RCT  AF 96-33-3, AE 145215-14-1
          RGT  AH 603-35-0 PPh3
          PRO  AG 145215-18-5
          CAT  3375-31-3 Pd(OAc)2

RX(17)    RCT  AG 145215-18-5
          RGT  AK 1310-73-2 NaOH
          PRO  AJ 145215-19-6

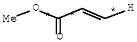

RX(175) OF 201 COMPOSED OF RX(9), RX(10), RX(11), RX(13), RX(15), RX(16),
          RX(17), RX(18)
RX(175)   S  +  2 V  +  AF  ===>  AL
```



S

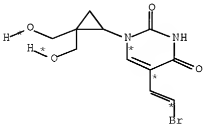


2 V



AF

8 STEPS →



AL

```
RX(9)     RCT  S 135345-90-3
          RGT  M 7664-41-7 NH3
```

```
             PRO   T 135345-91-4

RX(10)       RCT   T 135345-91-4
             PRO   U 135345-83-4
             NTE   H2/PD

RX(11)       RCT   U 135345-83-4, V 108-24-7
             PRO   W 145215-09-4

RX(13)       RCT   W 145215-09-4
             RGT   AA 10377-51-2 LiI
             PRO   Z 145215-11-8
             NTE   (NH4)2[CE(NO3)6]

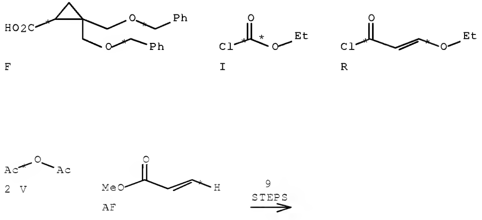
RX(15)       RCT   Z 145215-11-8
             RGT   AC 124-41-4 NaOMe
             PRO   AE 145215-14-1
             SOL   67-56-1 MeOH

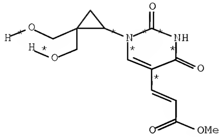
RX(16)       RCT   AF 96-33-3, AE 145215-14-1
             RGT   AH 603-35-0 PPh3
             PRO   AG 145215-18-5
             CAT   3375-31-3 Pd(OAc)2

RX(17)       RCT   AG 145215-18-5
             RGT   AK 1310-73-2 NaOH
             PRO   AJ 145215-19-6

RX(18)       RCT   AJ 145215-19-6
             RGT   AM 128-08-5 Bromosuccinimide
             PRO   AL 145215-20-9


RX(184) OF 201 COMPOSED OF RX(4), RX(5), RX(8), RX(9), RX(10), RX(11), RX(13),
             RX(15), RX(16)
RX(184)      F  +  I  +  R  +  2 V  +  AF  ===>  AG
```





AG

RX(4)   RCT F 135345-84-5, I 541-41-3
           RGT J 26628-22-8 NaN3
           PRO K 135345-85-6

RX(5)   RCT K 135345-85-6
           RGT M 7664-41-7 NH3
           PRO L 135345-89-0

RX(8)   RCT R 99471-66-6, L 135345-89-0
           PRO S 135345-90-3

RX(9)   RCT S 135345-90-3
           RGT M 7664-41-7 NH3
           PRO T 135345-91-4

RX(10)   RCT T 135345-91-4
           PRO U 135345-83-4
           NTE H2/PD

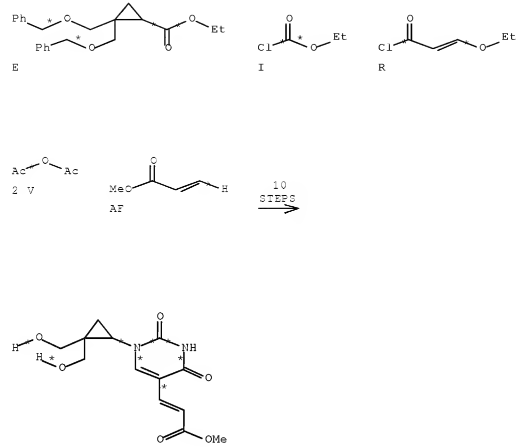
RX(11)   RCT U 135345-83-4, V 108-24-7
           PRO W 145215-09-4

RX(13)   RCT W 145215-09-4
           RGT AA 10377-51-2 LiI
           PRO Z 145215-11-8
           NTE (NH4)2[CE(NO3)6]

RX(15)   RCT Z 145215-11-8
           RGT AC 124-41-4 NaOMe
           PRO AE 145215-14-1
           SOL 67-56-1 MeOH

RX(16)   RCT AF 96-33-3, AE 145215-14-1
           RGT AH 603-35-0 PPh3
           PRO AG 145215-18-5
           CAT 3375-31-3 Pd(OAc)2

RX(186) OF 201 COMPOSED OF RX(2), RX(4), RX(5), RX(8), RX(9), RX(10), RX(11),
           RX(13), RX(15), RX(16)
RX(186)   E + I + R + 2 V + AF ===> AG



AG

```
RX(2)      RCT  E 145215-00-5
           RGT  G 1310-58-3 KOH
           PRO  F 135345-84-5

RX(4)      RCT  F 135345-84-5, I 541-41-3
           RGT  J 26628-22-8 NaN3
           PRO  K 135345-85-6

RX(5)      RCT  K 135345-85-6
           RGT  M 7664-41-7 NH3
           PRO  L 135345-89-0

RX(8)      RCT  R 99471-66-6, L 135345-89-0
           PRO  S 135345-90-3

RX(9)      RCT  S 135345-90-3
           RGT  M 7664-41-7 NH3
           PRO  T 135345-91-4

RX(10)     RCT  T 135345-91-4
           PRO  U 135345-83-4
           NTE  H2/PD

RX(11)     RCT  U 135345-83-4, V 108-24-7
```

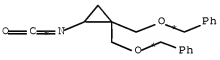
```
         PRO  W 145215-09-4

RX(13)   RCT  W 145215-09-4
         RGT  AA 10377-51-2 LiI
         PRO  Z 145215-11-8
         NTE  (NH4)2[CE(NO3)6]

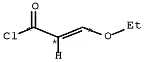
RX(15)   RCT  Z 145215-11-8
         RGT  AC 124-41-4 NaOMe
         PRO  AE 145215-14-1
         SOL  67-56-1 MeOH

RX(16)   RCT  AF 96-33-3, AE 145215-14-1
         RGT  AH 603-35-0 PPh3
         PRO  AG 145215-18-5
         CAT  3375-31-3 Pd(OAc)2

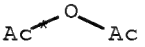

RX(188) OF 201 COMPOSED OF RX(5), RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),
         RX(16), RX(17)
RX(188)  K  +  R  +  2 V  +  AF  ===>  AJ
```



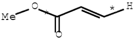
K



R

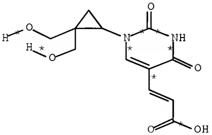


2 V



AF

9
STEPS
→



AJ

```
RX(5)    RCT  K 135345-85-6
         RGT  M 7664-41-7 NH3
```

```
          PRO   L 135345-89-0

RX(8)     RCT   R 99471-66-6, L 135345-89-0
          PRO   S 135345-90-3

RX(9)     RCT   S 135345-90-3
          RGT   M 7664-41-7 NH3
          PRO   T 135345-91-4

RX(10)    RCT   T 135345-91-4
          PRO   U 135345-83-4
          NTE   H2/PD

RX(11)    RCT   U 135345-83-4, V 108-24-7
          PRO   W 145215-09-4

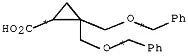
RX(13)    RCT   W 145215-09-4
          RGT   AA 10377-51-2 LiI
          PRO   Z 145215-11-8
          NTE   (NH4)2[CE(NO3)6]

RX(15)    RCT   Z 145215-11-8
          RGT   AC 124-41-4 NaOMe
          PRO   AE 145215-14-1
          SOL   67-56-1 MeOH

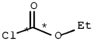
RX(16)    RCT   AF 96-33-3, AE 145215-14-1
          RGT   AH 603-35-0 PPh3
          PRO   AG 145215-18-5
          CAT   3375-31-3 Pd(OAc)2

RX(17)    RCT   AG 145215-18-5
          RGT   AK 1310-73-2 NaOH
          PRO   AJ 145215-19-6


RX(190) OF 201 COMPOSED OF RX(4), RX(5), RX(8), RX(9), RX(10), RX(11), RX(13),
          RX(15), RX(16), RX(17)
RX(190)   F  +  I  +  R  +  2 V  +  AF  ===>  AJ
```



F



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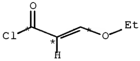
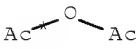
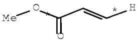


R

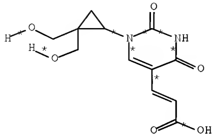


2 V



AF

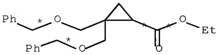
10
STEPS
$\longrightarrow$

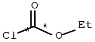


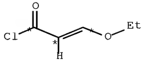
AJ

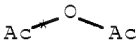
RX(4)	RCT	F 135345-84-5, I 541-41-3
	RGT	J 26628-22-8 NaN3
	PRO	K 135345-85-6
RX(5)	RCT	K 135345-85-6
	RGT	M 7664-41-7 NH3
	PRO	L 135345-89-0
RX(8)	RCT	R 99471-66-6, L 135345-89-0
	PRO	S 135345-90-3
RX(9)	RCT	S 135345-90-3
	RGT	M 7664-41-7 NH3
	PRO	T 135345-91-4
RX(10)	RCT	T 135345-91-4
	PRO	U 135345-83-4
	NTE	H2/PD
RX(11)	RCT	U 135345-83-4, V 108-24-7
	PRO	W 145215-09-4
RX(13)	RCT	W 145215-09-4
	RGT	AA 10377-51-2 LiI
	PRO	Z 145215-11-8
	NTE	(NH4)2[CE(NO3)6]
RX(15)	RCT	Z 145215-11-8
	RGT	AC 124-41-4 NaOMe
	PRO	AE 145215-14-1
	SOL	67-56-1 MeOH
RX(16)	RCT	AF 96-33-3, AE 145215-14-1
	RGT	AH 603-35-0 PPh3
	PRO	AG 145215-18-5
	CAT	3375-31-3 Pd(OAc)2
RX(17)	RCT	AG 145215-18-5
	RGT	AK 1310-73-2 NaOH
	PRO	AJ 145215-19-6

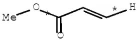
RX(192) OF 201 COMPOSED OF RX(2), RX(4), RX(5), RX(8), RX(9), RX(10), RX(11),
RX(13), RX(15), RX(16), RX(17)
RX(192) E + I + R + 2 V + AF ===> AJ


E

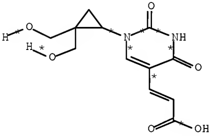

I


R


2 V


AF

11 STEPS
→


AJ

RX(2) RCT E 145215-00-5
RGT G 1310-58-3 KOH
PRO F 135345-84-5

RX(4) RCT F 135345-84-5, I 541-41-3
RGT J 26628-22-8 NaN3
PRO K 135345-85-6

RX(5) RCT K 135345-85-6
RGT M 7664-41-7 NH3
PRO L 135345-89-0

RX(8) RCT R 99471-66-6, L 135345-89-0
PRO S 135345-90-3

RX(9) RCT S 135345-90-3
RGT M 7664-41-7 NH3
PRO T 135345-91-4

```
RX(10)       RCT  T 135345-91-4
             PRO  U 135345-83-4
             NTE  H2/PD

RX(11)       RCT  U 135345-83-4, V 108-24-7
             PRO  W 145215-09-4

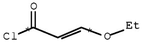
RX(13)       RCT  W 145215-09-4
             RGT  AA 10377-51-2 LiI
             PRO  Z 145215-11-8
             NTE  (NH4)2[CE(NO3)6]

RX(15)       RCT  Z 145215-11-8
             RGT  AC 124-41-4 NaOMe
             PRO  AE 145215-14-1
             SOL  67-56-1 MeOH

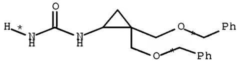
RX(16)       RCT  AF 96-33-3, AE 145215-14-1
             RGT  AH 603-35-0 PPh3
             PRO  AG 145215-18-5
             CAT  3375-31-3 Pd(OAc)2

RX(17)       RCT  AG 145215-18-5
             RGT  AK 1310-73-2 NaOH
             PRO  AJ 145215-19-6

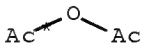

RX(194) OF 201 COMPOSED OF RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),
             RX(16), RX(17), RX(18)
RX(194)      P  +  L  +  2 V  +  AF  ===>  AL
```



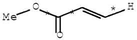
R



L

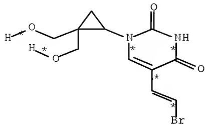


2 V



AF

9
STEPS
→



AL

```
RX(8)      RCT  R 99471-66-6, L 135345-89-0
           PRO  S 135345-90-3

RX(9)      RCT  S 135345-90-3
           RGT  M 7664-41-7 NH3
           PRO  T 135345-91-4

RX(10)     RCT  T 135345-91-4
           PRO  U 135345-83-4
           NTE  H2/PD

RX(11)     RCT  U 135345-83-4, V 108-24-7
           PRO  W 145215-09-4

RX(13)     RCT  W 145215-09-4
           RGT  AA 10377-51-2 LiI
           PRO  Z 145215-11-8
           NTE  (NH4)2[CE(NO3)6]

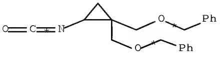
RX(15)     RCT  Z 145215-11-8
           RGT  AC 124-41-4 NaOMe
           PRO  AE 145215-14-1
           SOL  67-56-1 MeOH

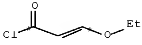
RX(16)     RCT  AF 96-33-3, AE 145215-14-1
           RGT  AH 603-35-0 PPh3
           PRO  AG 145215-18-5
           CAT  3375-31-3 Pd(OAc)2

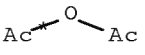
RX(17)     RCT  AG 145215-18-5
           RGT  AK 1310-73-2 NaOH
           PRO  AJ 145215-19-6

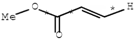
RX(18)     RCT  AJ 145215-19-6
           RGT  AM 128-08-5 Bromosuccinimide
           PRO  AL 145215-20-9


RX(196) OF 201 COMPOSED OF RX(5), RX(8), RX(9), RX(10), RX(11), RX(13), RX(15),
           RX(16), RX(17), RX(18)
RX(196)    K  +  R  +  2 V  +  AF  ===>  AL
```

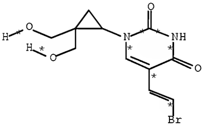

K


R


2 V


AF

10 STEPS →


AL

```
RX(5)     RCT  K 135345-85-6
          RGT  M 7664-41-7 NH3
          PRO  L 135345-89-0

RX(8)     RCT  R 99471-66-6, L 135345-89-0
          PRO  S 135345-90-3

RX(9)     RCT  S 135345-90-3
          RGT  M 7664-41-7 NH3
          PRO  T 135345-91-4

RX(10)    RCT  T 135345-91-4
          PRO  U 135345-83-4
          NTE  H2/PD

RX(11)    RCT  U 135345-83-4, V 108-24-7
          PRO  W 145215-09-4

RX(13)    RCT  W 145215-09-4
          RGT  AA 10377-51-2 LiI
          PRO  Z 145215-11-8
          NTE  (NH4)2[CE(NO3)6]

RX(15)    RCT  Z 145215-11-8
          RGT  AC 124-41-4 NaOMe
```

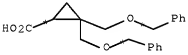
```
          PRO   AE 145215-14-1
          SOL   67-56-1 MeOH

RX(16)    RCT   AF 96-33-3, AE 145215-14-1
          RGT   AH 603-35-0 PPh3
          PRO   AG 145215-18-5
          CAT   3375-31-3 Pd(OAc)2

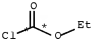
RX(17)    RCT   AG 145215-18-5
          RGT   AK 1310-73-2 NaOH
          PRO   AJ 145215-19-6

RX(18)    RCT   AJ 145215-19-6
          RGT   AM 128-08-5 Bromosuccinimide
          PRO   AL 145215-20-9

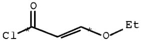

RX(198) OF 201 COMPOSED OF RX(4), RX(5), RX(8), RX(9), RX(10), RX(11), RX(13),
          RX(15), RX(16), RX(17), RX(18)
RX(198)   F  +  I  +  R  +  2 V  +  AF  ===>  AL
```



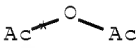
F



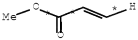
I



R

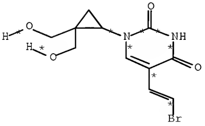


2 V



AF

11
STEPS



AL

```
RX(4)     RCT   F 135345-84-5, I 541-41-3
          RGT   J 26628-22-8 NaN3
          PRO   K 135345-85-6
```

```
RX(5)      RCT  K 135345-85-6
           RGT  M 7664-41-7 NH3
           PRO  L 135345-89-0

RX(8)      RCT  R 99471-66-6, L 135345-89-0
           PRO  S 135345-90-3

RX(9)      RCT  S 135345-90-3
           RGT  M 7664-41-7 NH3
           PRO  T 135345-91-4

RX(10)     RCT  T 135345-91-4
           PRO  U 135345-83-4
           NTE  H2/PD

RX(11)     RCT  U 135345-83-4, V 108-24-7
           PRO  W 145215-09-4

RX(13)     RCT  W 145215-09-4
           RGT  AA 10377-51-2 LiI
           PRO  Z 145215-11-8
           NTE  (NH4)2[CE(NO3)6]

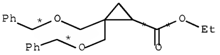
RX(15)     RCT  Z 145215-11-8
           RGT  AC 124-41-4 NaOMe
           PRO  AE 145215-14-1
           SOL  67-56-1 MeOH

RX(16)     RCT  AF 96-33-3, AE 145215-14-1
           RGT  AH 603-35-0 PPh3
           PRO  AG 145215-18-5
           CAT  3375-31-3 Pd(OAc)2

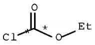
RX(17)     RCT  AG 145215-18-5
           RGT  AK 1310-73-2 NaOH
           PRO  AJ 145215-19-6

RX(18)     RCT  AJ 145215-19-6
           RGT  AM 128-08-5 Bromosuccinimide
           PRO  AL 145215-20-9

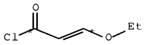

RX(200) OF 201 COMPOSED OF RX(2), RX(4), RX(5), RX(8), RX(9), RX(10), RX(11),
           RX(13), RX(15), RX(16), RX(17), RX(18)
RX(200)    E  +  I  +  R  +  2 V  +  AF  ===>  AL
```



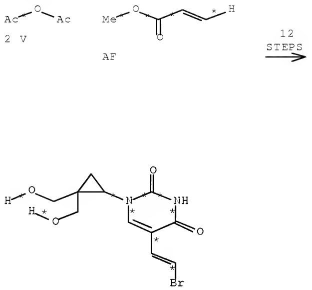
E



I



R



AL

```
RX(2)       RCT   E 145215-00-5
            RGT   G 1310-58-3 KOH
            PRO   F 135345-84-5

RX(4)       RCT   F 135345-84-5, I 541-41-3
            RGT   J 26628-22-8 NaN3
            PRO   K 135345-85-6

RX(5)       RCT   K 135345-85-6
            RGT   M 7664-41-7 NH3
            PRO   L 135345-89-0

RX(8)       RCT   R 99471-66-6, L 135345-89-0
            PRO   S 135345-90-3

RX(9)       RCT   S 135345-90-3
            RGT   M 7664-41-7 NH3
            PRO   T 135345-91-4

RX(10)      RCT   T 135345-91-4
            PRO   U 135345-83-4
            NTE   H2/PD

RX(11)      RCT   U 135345-83-4, V 108-24-7
            PRO   W 145215-09-4

RX(13)      RCT   W 145215-09-4
            RGT   AA 10377-51-2 LiI
            PRO   Z 145215-11-8
            NTE   (NH4)2[CE(NO3)6]

RX(15)      RCT   Z 145215-11-8
            RGT   AC 124-41-4 NaOMe
            PRO   AE 145215-14-1
```

SOL 67-56-1 MeOH

RX(16) RCT AF 96-33-3, AE 145215-14-1
RGT AH 603-35-0 PPh3
PRO AG 145215-18-5
CAT 3375-31-3 Pd(OAc)2

RX(17) RCT AG 145215-18-5
RGT AK 1310-73-2 NaOH
PRO AJ 145215-19-6

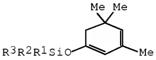
RX(18) RCT AJ 145215-19-6
RGT AM 128-08-5 Bromosuccinimide
PRO AL 145215-20-9

L46 ANSWER 15 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

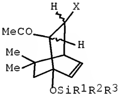
ACCESSION NUMBER: 117:48950 CASREACT Full-text
TITLE: Preparation of 3-oxo-α-ionone
INVENTOR(S): Ito, Nobuhiko; Kinoshita, Kimio; Eto, Takeaki
PATENT ASSIGNEE(S): Soda Aromatic Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04041455	A	19920212	JP 1990-146361	19900606
JP 2929218	B2	19990803		

PRIORITY APPLN. INFO.: JP 1990-146361 19900606
OTHER SOURCE(S): MARPAT 117:48950
GI



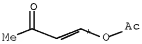
III



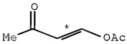
IV

AB The title compound (I) is prepared by treating XCH:CHCOMe (II; X = alkoxy, acyloxy) with cyclohexadienes III (R1-R3 = C1-5 aliphatic hydrocarbyl) in the presence of Lewis acids, then optional treating with acids. Bicyclooctenes IV, useful as intermediates for I, are also prepared A solution of AlCl3 in CH2Cl2 was treated dropwise with a solution of II (X = AcO) in CH2Cl2 at -3° over 2 min, then with a solution of III (R1 = R2 = R3 = Me) in CH2Cl2 over 13 min, and stirred at -3° for 2 h to give a mixture containing I 39.3, 7-endo-8-exo-IV 23.6, 7-exo-8-endo-IV 29.2%.

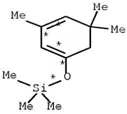
RX(1) OF 6   3 A + 3 B ===> C + D +
E...



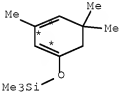
A



2 A

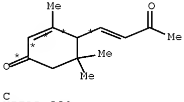


B

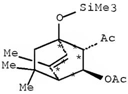


2 B

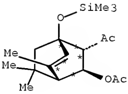
(1) →



C
YIELD 39%



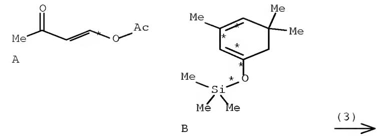
D
YIELD 23%

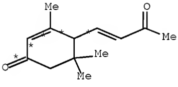


E
YIELD 29%

RX(1)   RCT A 13945-19-2, B 80699-65-6
          PRO C 20194-68-7, D 141915-26-6, E 141979-75-1
          CAT 7446-70-0 AlCl3
          SOL 75-09-2 CH2Cl2

RX(3) OF 6   A + B ===> C





C
YIELD 71%

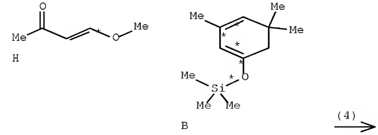
```
RX(3)      RCT  A 13945-19-2, B 80699-65-6

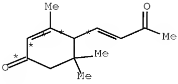
             STAGE(1)
                CAT  7446-70-0 AlCl3
                SOL  75-09-2 CH2Cl2

             STAGE(2)
                RGT  L 7664-93-9 H2SO4
                SOL  7732-18-5 Water, 67-56-1 MeOH

           PRO  C 20194-68-7

RX(4) OF 6      H  +  B  ===>  C
```





C
YIELD 67%

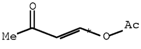
RX(4) RCT H 4652-27-1, B 80699-65-6

STAGE(1)
CAT 7446-70-0 AlCl3
SOL 75-09-2 CH2Cl2

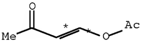
STAGE(2)
RGT L 7664-93-9 H2SO4
SOL 7732-18-5 Water, 67-56-1 MeOH

PRO C 20194-68-7

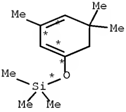
RX(6) OF 6 COMPOSED OF RX(1), RX(5)
RX(6) 3 A + 3 B ===> 2 C



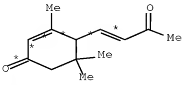
A



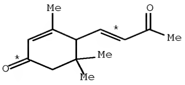
2 A



3 B



C
YIELD 96%

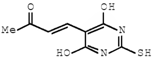


C
YIELD 96%

RX(1) RCT A 13945-19-2, B 80699-65-6
PRO C 20194-68-7, D 141915-26-6, E 141979-75-1
CAT 7446-70-0 AlCl3
SOL 75-09-2 CH2Cl2

RX(5) RCT D 141915-26-6, E 141979-75-1
RGT L 7664-93-9 H2SO4
PRO C 20194-68-7
SOL 7732-18-5 Water, 67-56-1 MeOH

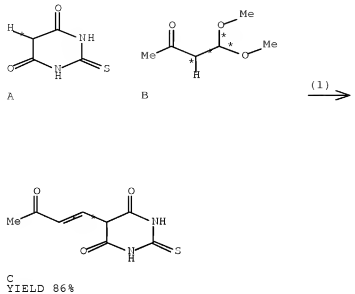
L46 ANSWER 16 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 111:233390 CASREACT Full-text
TITLE: A colorimetric method for the estimation of 2-deoxy-3-C-methyl-branched sugars
AUTHOR(S): Lo, Stanley F.; Yu, Yuan; Yang, Ding Yah; Liu, Hung Wen
CORPORATE SOURCE: Dep. Chem., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Carbohydrate Research (1989), 189, 368-73
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The title method is based on the oxidation of the 2-deoxy-3-C-methyl-branched sugars, e.g., L-mycarose, with NaIO4 and condensation of the MeCOCH2CHO formed with 2-thiobarbituric acid to give pyrimidine derivative I, which can be quantified spectrophotometrically at 372 nm.

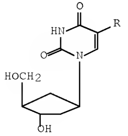
RX(1) OF 1 A + B ===> C



YIELD 86%

```
RX(1)     RCT  A 504-17-6, B 5436-21-5
          RGT  D 7647-01-0 HCl
          PRO  C 123765-14-0
```

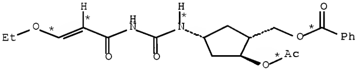
```
L46  ANSWER 17 OF 24  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        111:58252  CASREACT  Full-text
TITLE:                   Synthesis and antiviral activity of the enantiomeric
                         forms of carba-5-iodo-2'-deoxyuridine and
                         carba-(E)-5-(2-bromovinyl)-2'-deoxyuridine
AUTHOR(S):               Balzarini, Jan; Baumgartner, Harald; Bodenteich,
                         Michael; De Clercq, Erik; Griengl, Herfried
CORPORATE SOURCE:        Inst. Org. Chem., Graz Univ. Technol., Graz, A-8010,
                         Austria
SOURCE:                  Journal of Medicinal Chemistry (1989), 32(8), 1861-5
                         CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:           Journal
LANGUAGE:                English
GI
```



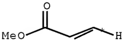
I

AB Both enantiomers of the carbocyclic analogs of 5-iodo-2'-deoxyuridine [(+)-I and (-)-I; R = iodo] and of (E)-5-(2-bromovinyl)-2'-deoxyuridine [(+)-I and (-)-I; R = (E)-CH:CHBr] were synthesized by using (+)- or (-)-endo-norborn-5-en-2-yl acetate or butyrate, resp., as starting materials. Against herpes simplex virus type 1, (+)-I (R = (E)-CH;CHBr](+)-C-BVDU] was only slightly less active than BVDU itself, whereas (-)-I [R = (E)-CH:CHBr][(-)-C-BVDU] proved to be 10-400-fold less effective, depending on the strain investigated. Against HSV-2 both (+)- and (-)-C-BVDU as well as (+)- and (-)-C-IDU showed minor activity. All carbocyclic analogs were inactive against TK- HSV-1 strains, pointing to the prerequisite of phosphorylation (activation) by the viral thymidine kinase.

RX(100) OF 267 COMPOSED OF RX(21), RX(23), RX(25)
RX(100) AW + BF ===> BG

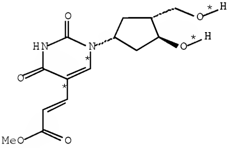


AW



BF

3 STEPS →



BG
YIELD 72%

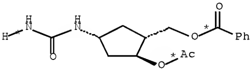
RX(21) RCT AW 120905-35-3

RGT AS 7664-41-7 NH3
PRO AY 120963-43-1
SOL 7732-18-5 Water

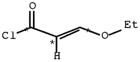
RX(23) RCT AY 120963-43-1
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3
PRO BA 114179-59-8
SOL 123-91-1 Dioxane

RX(25) RCT BA 114179-59-8, BF 96-33-3
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
PRO BG 120963-46-4
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

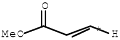
RX(101) OF 267 COMPOSED OF RX(19), RX(21), RX(23), RX(25)
RX(101) AQ + AV + BF ===> BG



AQ

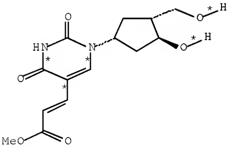


AV



BF

4 STEPS →



BG
YIELD 72%

RX(19) RCT AQ 120905-34-2, AV 6191-99-7
RGT V 110-86-1 Pyridine

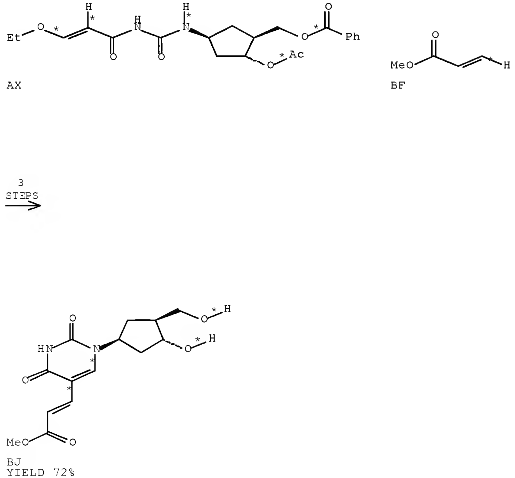
```
            PRO   AW 120905-35-3
            SOL   75-09-2 CH2Cl2

RX(21)      RCT   AW 120905-35-3
            RGT   AS 7664-41-7 NH3
            PRO   AY 120963-43-1
            SOL   7732-18-5 Water

RX(23)      RCT   AY 120963-43-1
            RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO   BA 114179-59-8
            SOL   123-91-1 Dioxane

RX(25)      RCT   BA 114179-59-8, BF 96-33-3
            RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO   BG 120963-46-4
            CAT   3375-31-3 Pd(OAc)2
            SOL   123-91-1 Dioxane


RX(102) OF 267 COMPOSED OF RX(22), RX(24), RX(26)
RX(102)    AX  +  BF  ===>  BJ
```



AX

BF

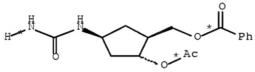
BJ
YIELD 72%

```
RX(22)      RCT  AX 120963-42-0
            RGT  AS 7664-41-7 NH3
            PRO  AZ 120963-44-2
            SOL  7732-18-5 Water

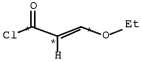
RX(24)      RCT  AZ 120963-44-2
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BE 120963-45-3
            SOL  123-91-1 Dioxane

RX(26)      RCT  BE 120963-45-3, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BJ 120963-47-5
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane

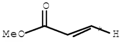

RX(103) OF 267 COMPOSED OF RX(20), RX(22), RX(24), RX(26)
RX(103)   AU  +  AV  +  BF  ===>  BJ
```



AU

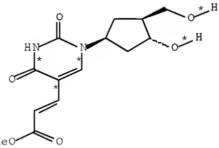


AV



BF

4 STEPS →



BJ
YIELD 72%

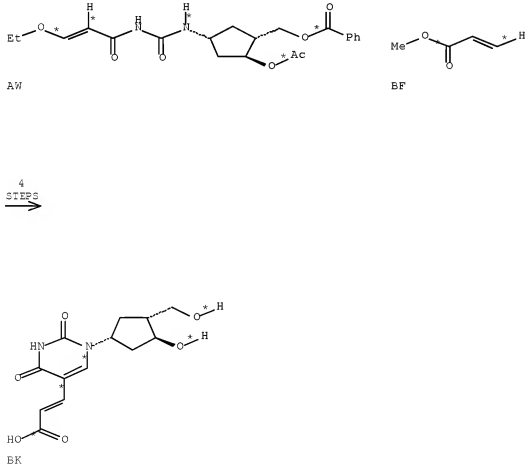
```
RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AX 120963-42-0
            SOL  75-09-2 CH2Cl2

RX(22)      RCT  AX 120963-42-0
            RGT  AS 7664-41-7 NH3
            PRO  AZ 120963-44-2
            SOL  7732-18-5 Water

RX(24)      RCT  AZ 120963-44-2
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BE 120963-45-3
            SOL  123-91-1 Dioxane

RX(26)      RCT  BE 120963-45-3, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BJ 120963-47-5
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane


RX(105) OF 267 COMPOSED OF RX(21), RX(23), RX(25), RX(27)
RX(105)    AW   +  BF   ===>  BK
```



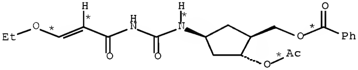
```
RX(21)      RCT   AW 120905-35-3
            RGT   AS 7664-41-7 NH3
            PRO   AY 120963-43-1
            SOL   7732-18-5 Water

RX(23)      RCT   AY 120963-43-1
            RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO   BA 114179-59-8
            SOL   123-91-1 Dioxane

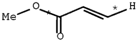
RX(25)      RCT   BA 114179-59-8, BF 96-33-3
            RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO   BG 120963-46-4
            CAT   3375-31-3 Pd(OAc)2
            SOL   123-91-1 Dioxane

RX(27)      RCT   BG 120963-46-4
            RGT   BL 1310-58-3 KOH
            PRO   BK 120963-48-6


RX(107) OF 267 COMPOSED OF RX(22), RX(24), RX(26), RX(28)
RX(107)    AX  +  BF  ===>  BM
```

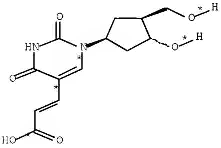


AX



BF

4
STEPS
→



BM

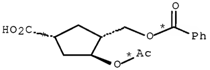
```
RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

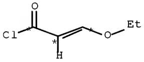
RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(28)     RCT  BJ 120963-47-5
           RGT  BL 1310-58-3 KOH
           PRO  BM 120963-49-7

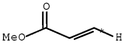

RX(172) OF 267 COMPOSED OF RX(17), RX(19), RX(21), RX(23), RX(25)
RX(172)   AN  +  AV  +  BF  ===>  BG
```



AN

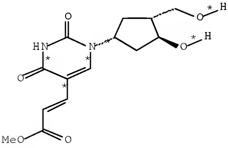


AV



BF

5
STEPS
→



BG
YIELD 72%

```
RX(17)     RCT   AN 120905-33-1

             STAGE(1)
                RGT   AR 26386-88-9 (PhO)2P(O)N3
                SOL   71-43-2 Benzene

             STAGE(2)
                RGT   AS 7664-41-7 NH3

           PRO   AQ 120905-34-2

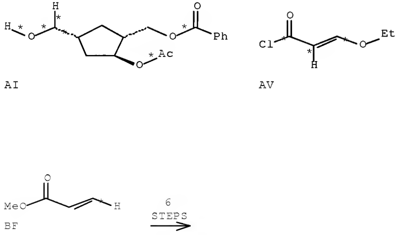
RX(19)     RCT   AQ 120905-34-2, AV 6191-99-7
           RGT   V 110-86-1 Pyridine
           PRO   AW 120905-35-3
           SOL   75-09-2 CH2Cl2

RX(21)     RCT   AW 120905-35-3
           RGT   AS 7664-41-7 NH3
           PRO   AY 120963-43-1
           SOL   7732-18-5 Water

RX(23)     RCT   AY 120963-43-1
           RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO   BA 114179-59-8
           SOL   123-91-1 Dioxane

RX(25)     RCT   BA 114179-59-8, BF 96-33-3
           RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO   BG 120963-46-4
           CAT   3375-31-3 Pd(OAc)2
           SOL   123-91-1 Dioxane

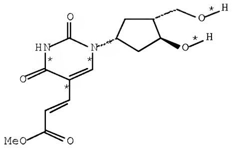

RX(173) OF 267 COMPOSED OF RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)
RX(173)    AI  +  AV  +  BF  ===>  BG
```



AI

AV

BF



BG
YIELD 72%

RX(15) RCT AI 120905-32-0
        RGT AO 20039-37-6 PDC
        PRO AN 120905-33-1
        SOL 68-12-2 DMF

RX(17) RCT AN 120905-33-1

  STAGE(1)
    RGT AR 26386-88-9 (PhO)2P(O)N3
    SOL 71-43-2 Benzene

  STAGE(2)
    RGT AS 7664-41-7 NH3

        PRO AQ 120905-34-2

RX(19) RCT AQ 120905-34-2, AV 6191-99-7
        RGT V 110-86-1 Pyridine
        PRO AW 120905-35-3
        SOL 75-09-2 CH2Cl2

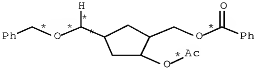
RX(21) RCT AW 120905-35-3
        RGT AS 7664-41-7 NH3
        PRO AY 120963-43-1
        SOL 7732-18-5 Water

RX(23) RCT AY 120963-43-1
        RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3
        PRO BA 114179-59-8
        SOL 123-91-1 Dioxane

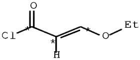
RX(25) RCT BA 114179-59-8, BF 96-33-3
        RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
        PRO BG 120963-46-4
        CAT 3375-31-3 Pd(OAc)2
        SOL 123-91-1 Dioxane

RX(174) OF 267 COMPOSED OF RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)

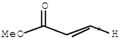
RX(174) AC + AV + BF ===> BG



AC

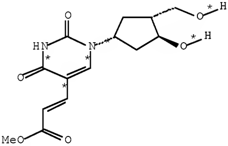


AV



BF

7
STEPS



BG
YIELD 72%

```
RX(13)     RCT   AC 120905-29-5
           RGT   AJ 1333-74-0 H2
           PRO   AI 120905-32-0
           CAT   7440-05-3 Pd
           SOL   64-17-5 EtOH

RX(15)     RCT   AI 120905-32-0
           RGT   AO 20039-37-6 PDC
           PRO   AN 120905-33-1
           SOL   68-12-2 DMF

RX(17)     RCT   AN 120905-33-1

             STAGE(1)
                RGT   AR 26386-88-9 (PhO)2P(O)N3
                SOL   71-43-2 Benzene

             STAGE(2)
                RGT   AS 7664-41-7 NH3
```

```
         PRO  AQ 120905-34-2

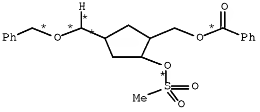
RX(19)   RCT  AQ 120905-34-2, AV 6191-99-7
         RGT  V 110-86-1 Pyridine
         PRO  AW 120905-35-3
         SOL  75-09-2 CH2Cl2

RX(21)   RCT  AW 120905-35-3
         RGT  AS 7664-41-7 NH3
         PRO  AY 120963-43-1
         SOL  7732-18-5 Water

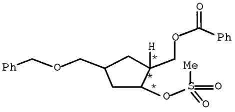
RX(23)   RCT  AY 120963-43-1
         RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
         PRO  BA 114179-59-8
         SOL  123-91-1 Dioxane

RX(25)   RCT  BA 114179-59-8, BF 96-33-3
         RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
         PRO  BG 120963-46-4
         CAT  3375-31-3 Pd(OAc)2
         SOL  123-91-1 Dioxane

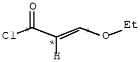

RX(175) OF 267 COMPOSED OF RX(11), RX(13), RX(15), RX(17), RX(19), RX(21),
         RX(23), RX(25)
RX(175)  2 Z  +  AV  +  BF  ===>  BG
```



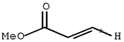
Z



Z

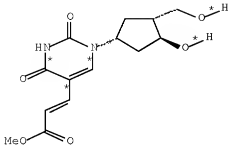


AV



BF

8 STEPS →



BG
YIELD 72%

```
RX(11)     RCT  Z 116142-70-2
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AC 120905-29-5, AD 120905-30-8
           SOL  67-68-5 DMSO

RX(13)     RCT  AC 120905-29-5
           RGT  AJ 1333-74-0 H2
           PRO  AI 120905-32-0
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(15)     RCT  AI 120905-32-0
           RGT  AO 20039-37-6 PDC
           PRO  AN 120905-33-1
           SOL  68-12-2 DMF

RX(17)     RCT  AN 120905-33-1

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

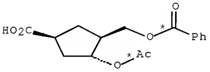
RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

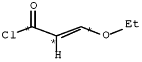
RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane
```

```
RX(25)      RCT  BA 114179-59-8, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BG 120963-46-4
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane

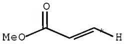

RX(176) OF 267 COMPOSED OF RX(18), RX(20), RX(22), RX(24), RX(26)
RX(176)    AP  +  AV  +  BF  ===>  BJ
```



AP

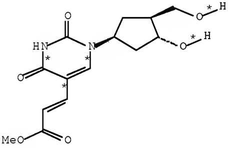


AV



BF

5
STEPS
→



BJ
YIELD 72%

```
RX(18)      RCT  AP 120963-40-8

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AU 120963-41-9

RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
```

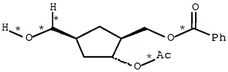
```
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

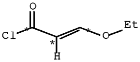
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

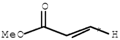

RX(177) OF 267 COMPOSED OF RX(16), RX(18), RX(20), RX(22), RX(24), RX(26)
RX(177)   AM  +  AV  +  BF  ===>  BJ
```



AM

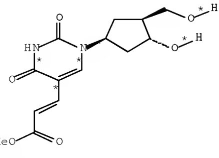


AV



BF

6
STEPS
→



BJ
YIELD 72%

```
RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

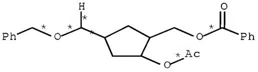
RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

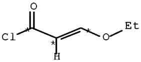
RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

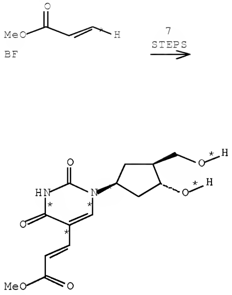

RX(178) OF 267 COMPOSED OF RX(14), RX(16), RX(18), RX(20), RX(22), RX(24),
           RX(26)
RX(178)    AG  +  AV  +  BF  ===>  BJ
```



AG



AV



BF

BJ
YIELD 72%

```
RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

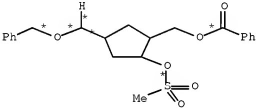
RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
```

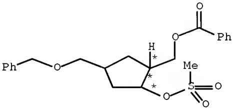
```
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BE 120963-45-3
          SOL   123-91-1 Dioxane

RX(26)    RCT   BE 120963-45-3, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BJ 120963-47-5
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

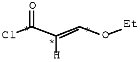

RX(179) OF 267 COMPOSED OF RX(12), RX(14), RX(16), RX(18), RX(20), RX(22),
          RX(24), RX(26)
RX(179)   2 AB  +  AV  +  BF  ===>  BJ
```



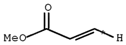
AB



AB

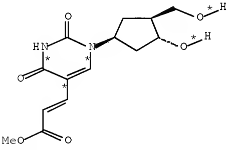


AV



BF

8 STEPS →



BJ
YIELD 72%

```
RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

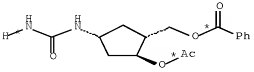
RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

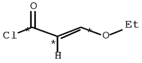
RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

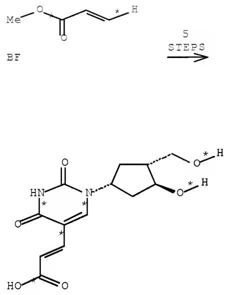

RX(180) OF 267 COMPOSED OF RX(19), RX(21), RX(23), RX(25), RX(27)
RX(180)    AQ  +  AV  +  BF  ===>  BK
```



AQ



AV



BF

BK

```
RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

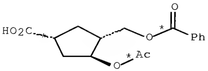
RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

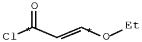
RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(27)     RCT  BG 120963-46-4
           RGT  BL 1310-58-3 KOH
           PRO  BK 120963-48-6

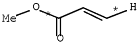
RX(181) OF 267 COMPOSED OF RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)
RX(181)   AN  +  AV  +  BF  ===>  BK
```



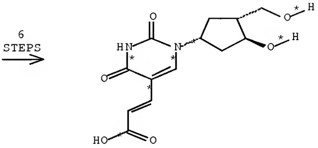
AN



AV



BF



BK

```
RX(17)   RCT  AN 120905-33-1

           STAGE(1)
              RGT  AR 26386-88-9 (PhO)2P(O)N3
              SOL  71-43-2 Benzene

           STAGE(2)
              RGT  AS 7664-41-7 NH3

         PRO  AQ 120905-34-2

RX(19)   RCT  AQ 120905-34-2, AV 6191-99-7
         RGT  V 110-86-1 Pyridine
         PRO  AW 120905-35-3
         SOL  75-09-2 CH2Cl2

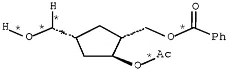
RX(21)   RCT  AW 120905-35-3
         RGT  AS 7664-41-7 NH3
         PRO  AY 120963-43-1
         SOL  7732-18-5 Water

RX(23)   RCT  AY 120963-43-1
         RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
         PRO  BA 114179-59-8
         SOL  123-91-1 Dioxane

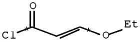
RX(25)   RCT  BA 114179-59-8, BF 96-33-3
         RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
         PRO  BG 120963-46-4
         CAT  3375-31-3 Pd(OAc)2
         SOL  123-91-1 Dioxane
```

```
RX(27)      RCT  BG 120963-46-4
            RGT  BL 1310-58-3 KOH
            PRO  BK 120963-48-6

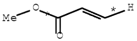

RX(182) OF 267 COMPOSED OF RX(15), RX(17), RX(19), RX(21), RX(23), RX(25),
            RX(27)
RX(182)     AI   +   AV   +   BF   ===>   BK
```



AI

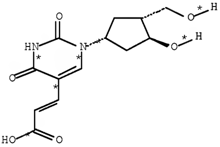


AV



BF

7
STEPS



BK

```
RX(15)      RCT  AI 120905-32-0
            RGT  AO 20039-37-6 PDC
            PRO  AN 120905-33-1
            SOL  68-12-2 DMF

RX(17)      RCT  AN 120905-33-1

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
```

```
                RGT  AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

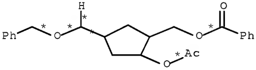
RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

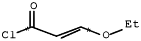
RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(27)     RCT  BG 120963-46-4
           RGT  BL 1310-58-3 KOH
           PRO  BK 120963-48-6

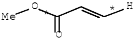

RX(183) OF 267 COMPOSED OF RX(13), RX(15), RX(17), RX(19), RX(21), RX(23),
           RX(25), RX(27)
RX(183)    AC  +  AV  +  BF  ===>  BK
```



AC

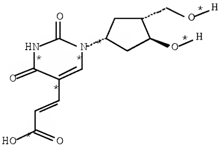


AV



BF

8
STEPS
→



BK

```
RX(13)     RCT  AC 120905-29-5
           RGT  AJ 1333-74-0 H2
           PRO  AI 120905-32-0
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(15)     RCT  AI 120905-32-0
           RGT  AO 20039-37-6 PDC
           PRO  AN 120905-33-1
           SOL  68-12-2 DMF

RX(17)     RCT  AN 120905-33-1

             STAGE(1)
                RGT   AR 26386-88-9 (PhO)2P(O)N3
                SOL   71-43-2 Benzene

             STAGE(2)
                RGT   AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

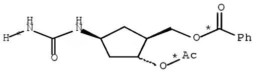
RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

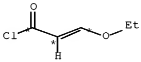
RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane
```

```
RX(27)      RCT  BG 120963-46-4
            RGT  BL 1310-58-3 KOH
            PRO  BK 120963-48-6

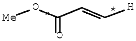

RX(184) OF 267 COMPOSED OF RX(20), RX(22), RX(24), RX(26), RX(28)
RX(184)    AU  +  AV  +  BF  ===>  BM
```



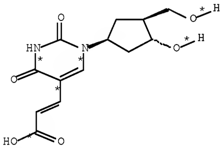
AU



AV



BF



BM

```
RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AX 120963-42-0
            SOL  75-09-2 CH2Cl2

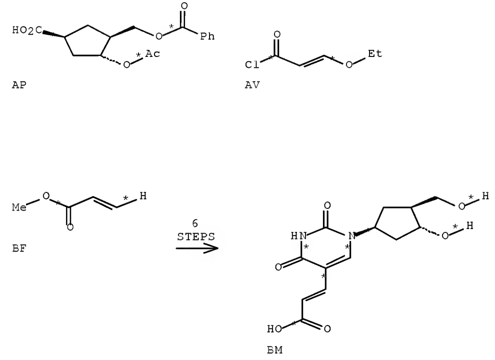
RX(22)      RCT  AX 120963-42-0
            RGT  AS 7664-41-7 NH3
            PRO  AZ 120963-44-2
            SOL  7732-18-5 Water

RX(24)      RCT  AZ 120963-44-2
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BE 120963-45-3
            SOL  123-91-1 Dioxane
```

RX(26) RCT BE 120963-45-3, BF 96-33-3
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
PRO BJ 120963-47-5
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5
RGT BL 1310-58-3 KOH
PRO BM 120963-49-7

RX(185) OF 267 COMPOSED OF RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)
RX(185) AP + AV + BF ===> BM



RX(18) RCT AP 120963-40-8

STAGE(1)
RGT AR 26386-88-9 (PhO)2P(O)N3
SOL 71-43-2 Benzene

STAGE(2)
RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7
RGT V 110-86-1 Pyridine
PRO AX 120963-42-0
SOL 75-09-2 CH2Cl2

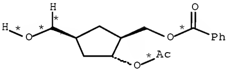
```
RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

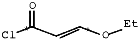
RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(28)     RCT  BJ 120963-47-5
           RGT  BL 1310-58-3 KOH
           PRO  BM 120963-49-7

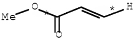

RX(186) OF 267 COMPOSED OF RX(16), RX(18), RX(20), RX(22), RX(24), RX(26),
           RX(28)
RX(186)    AM  +  AV  +  BF  ===>  BM
```



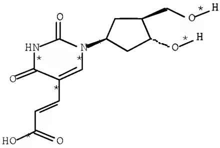
AM



AV



BF



BM

```
RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

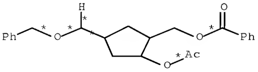
RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

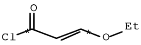
RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(28)     RCT  BJ 120963-47-5
           RGT  BL 1310-58-3 KOH
           PRO  BM 120963-49-7

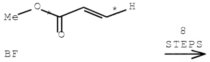

RX(187) OF 267 COMPOSED OF RX(14), RX(16), RX(18), RX(20), RX(22), RX(24),
           RX(26), RX(28)
RX(187)    AG  +  AV  +  BF  ===>  BM
```



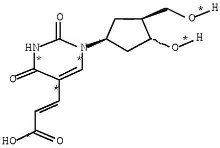
AG



AV



BF



BM

```
RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

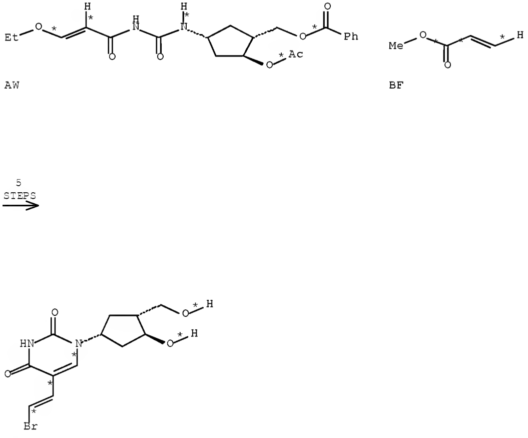
RX(24)    RCT  AZ 120963-44-2
```

```
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(28)    RCT  BJ 120963-47-5
          RGT  BL 1310-58-3 KOH
          PRO  BM 120963-49-7


RX(188) OF 267 COMPOSED OF RX(21), RX(23), RX(25), RX(27), RX(29)
RX(188)   AW  +  BF  ===>  BN
```



BN

```
RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
```

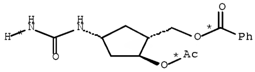
```
          PRO   BA 114179-59-8
          SOL   123-91-1 Dioxane

RX(25)    RCT   BA 114179-59-8, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BG 120963-46-4
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

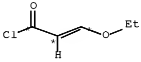
RX(27)    RCT   BG 120963-46-4
          RGT   BL 1310-58-3 KOH
          PRO   BK 120963-48-6

RX(29)    RCT   BK 120963-48-6
          RGT   BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO   BN 95463-56-2
          SOL   68-12-2 DMF

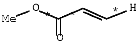

RX(189) OF 267 COMPOSED OF RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)
RX(189)    AQ  +  AV  +  BF  ===>  BN
```



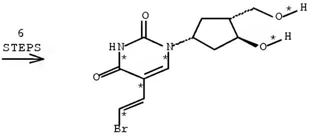
AQ



AV



BF



BN

```
RX(19)    RCT   AQ 120905-34-2, AV 6191-99-7
          RGT   V 110-86-1 Pyridine
          PRO   AW 120905-35-3
          SOL   75-09-2 CH2Cl2

RX(21)    RCT   AW 120905-35-3
          RGT   AS 7664-41-7 NH3
          PRO   AY 120963-43-1
          SOL   7732-18-5 Water
```

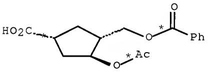
```
RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

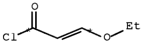
RX(27)     RCT  BG 120963-46-4
           RGT  BL 1310-58-3 KOH
           PRO  BK 120963-48-6

RX(29)     RCT  BK 120963-48-6
           RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
           PRO  BN 95463-56-2
           SOL  68-12-2 DMF

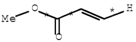

RX(190) OF 267 COMPOSED OF RX(17), RX(19), RX(21), RX(23), RX(25), RX(27),
           RX(29)
RX(190)    AN  +  AV  +  BF  ===>  BN
```



AN

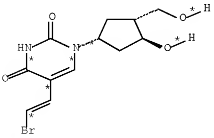


AV



BF

7 STEPS



BN

```
RX(17)     RCT  AN 120905-33-1

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

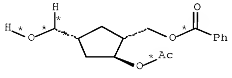
RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

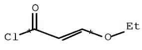
RX(27)     RCT  BG 120963-46-4
           RGT  BL 1310-58-3 KOH
           PRO  BK 120963-48-6

RX(29)     RCT  BK 120963-48-6
           RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
           PRO  BN 95463-56-2
           SOL  68-12-2 DMF

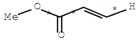

RX(191) OF 267 COMPOSED OF RX(15), RX(17), RX(19), RX(21), RX(23), RX(25),
           RX(27), RX(29)
RX(191)    AI  +  AV  +  BF  ===>  BN
```



AI

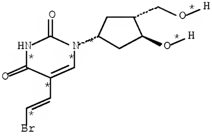


AV



BF

8
STEPS
→



BN

```
RX(15)     RCT  AI 120905-32-0
           RGT  AO 20039-37-6 PDC
           PRO  AN 120905-33-1
           SOL  68-12-2 DMF

RX(17)     RCT  AN 120905-33-1

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

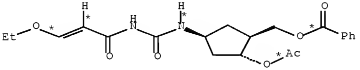
RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
```

```
          SOL  123-91-1 Dioxane

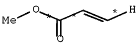
RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6

RX(29)    RCT  BK 120963-48-6
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BN 95463-56-2
          SOL  68-12-2 DMF

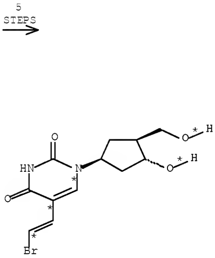

RX(192) OF 267 COMPOSED OF RX(22), RX(24), RX(26), RX(28), RX(30)
RX(192)   AX  +  BF  ===>  BQ
```



AX



BF



BQ

```
RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

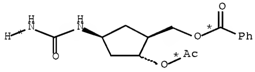
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane
```

```
RX(26)      RCT  BE 120963-45-3, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BJ 120963-47-5
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane

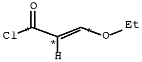
RX(28)      RCT  BJ 120963-47-5
            RGT  BL 1310-58-3 KOH
            PRO  BM 120963-49-7

RX(30)      RCT  BM 120963-49-7
            RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
            PRO  BQ 120963-50-0
            SOL  68-12-2 DMF

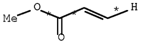

RX(193) OF 267 COMPOSED OF RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(193)    AU  +  AV  +  BF  ===>  BQ
```



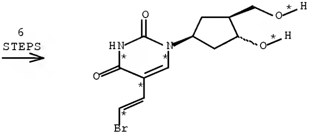
AU



AV



BF



BQ

```
RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AX 120963-42-0
            SOL  75-09-2 CH2Cl2

RX(22)      RCT  AX 120963-42-0
            RGT  AS 7664-41-7 NH3
            PRO  AZ 120963-44-2
            SOL  7732-18-5 Water

RX(24)      RCT  AZ 120963-44-2
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BE 120963-45-3
```

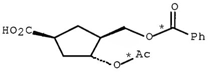
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
PRO BJ 120963-47-5
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

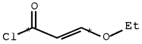
RX(28) RCT BJ 120963-47-5
RGT BL 1310-58-3 KOH
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
PRO BQ 120963-50-0
SOL 68-12-2 DMF

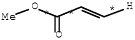
RX(194) OF 267 COMPOSED OF RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(194) AP + AV + BF ===> BQ



AP

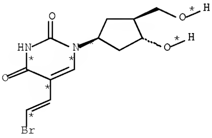


AV



BF

7 STEPS ⟶



BQ

RX(18) RCT AP 120963-40-8

```
            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

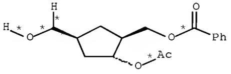
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

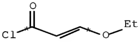
RX(28)    RCT  BJ 120963-47-5
          RGT  BL 1310-58-3 KOH
          PRO  BM 120963-49-7

RX(30)    RCT  BM 120963-49-7
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BQ 120963-50-0
          SOL  68-12-2 DMF

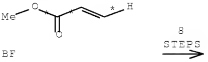

RX(195) OF 267 COMPOSED OF RX(16), RX(18), RX(20), RX(22), RX(24), RX(26),
          RX(28), RX(30)
RX(195)   AM  +  AV  +  BF  ===>  BQ
```



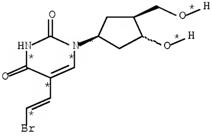
AM



AV



BF



BQ

```
RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
```

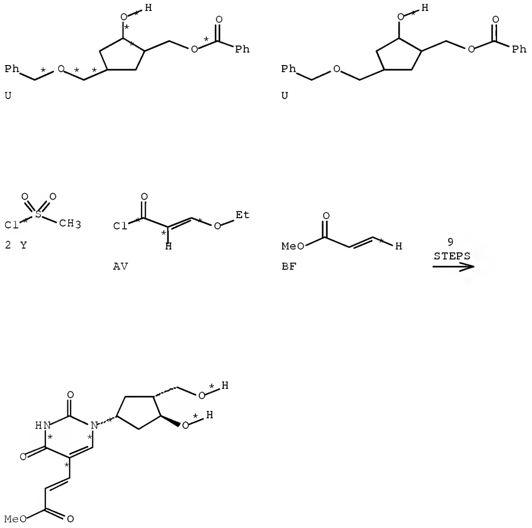
SOL 123-91-1 Dioxane

RX(28) RCT BJ 120963-47-5
RGT BL 1310-58-3 KOH
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
PRO BQ 120963-50-0
SOL 68-12-2 DMF

RX(226) OF 267 COMPOSED OF RX(9), RX(11), RX(13), RX(15), RX(17), RX(19),
RX(21), RX(23), RX(25)

RX(226) 2 U + 2 Y + AV + BF ===> BG



BG
YIELD 72%

RX(9) RCT U 120236-99-9, Y 124-63-0

```
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

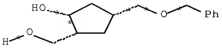
RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

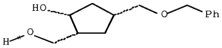
RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

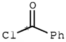

RX(227) OF 267 COMPOSED OF RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),
          RX(19), RX(21), RX(23), RX(25)
RX(227)   2 P  +  2 T  +  2 Y  +  AV  +  BF  ===>
          BG
```



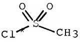
P



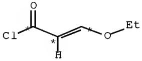
P



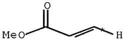
2 T



2 Y

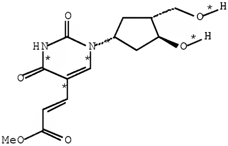


AV



BF

$\xrightarrow[\text{}]{\text{10 STEPS}}$



BG
YIELD 72%

```
RX(7)      RCT  P 120236-98-8, T 98-88-4
           RGT  V 110-86-1 Pyridine
           PRO  U 120236-99-9
           SOL  75-09-2 CH2Cl2

RX(9)      RCT  U 120236-99-9, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  Z 116142-70-2
           SOL  75-09-2 CH2Cl2

RX(11)     RCT  Z 116142-70-2
```

```
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

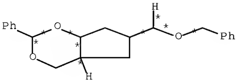
RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

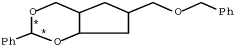
RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

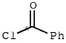

RX(228) OF 267 COMPOSED OF RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),
          RX(19), RX(21), RX(23), RX(25)
RX(228)   2 N  +  2 T  +  2 Y  +  AV  +  BF  ===>
          BG
```



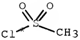
N



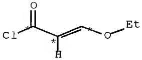
N



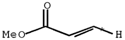
2 T



2 Y

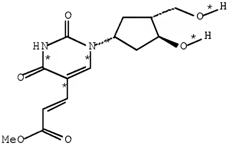


AV



BF

11
STEPS
→



BG
YIELD 72%

```
RX(5)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  P 120236-98-8
          SOL  7732-18-5 Water

RX(7)     RCT  P 120236-98-8, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2
```

```
RX(9)       RCT  U 120236-99-9, Y 124-63-0
            RGT  AA 121-44-8 Et3N
            PRO  Z 116142-70-2
            SOL  75-09-2 CH2Cl2

RX(11)      RCT  Z 116142-70-2
            RGT  AE 3396-11-0 Cs(OAc)2
            PRO  AC 120905-29-5, AD 120905-30-8
            SOL  67-68-5 DMSO

RX(13)      RCT  AC 120905-29-5
            RGT  AJ 1333-74-0 H2
            PRO  AI 120905-32-0
            CAT  7440-05-3 Pd
            SOL  64-17-5 EtOH

RX(15)      RCT  AI 120905-32-0
            RGT  AO 20039-37-6 PDC
            PRO  AN 120905-33-1
            SOL  68-12-2 DMF

RX(17)      RCT  AN 120905-33-1

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AQ 120905-34-2

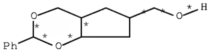
RX(19)      RCT  AQ 120905-34-2, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AW 120905-35-3
            SOL  75-09-2 CH2Cl2

RX(21)      RCT  AW 120905-35-3
            RGT  AS 7664-41-7 NH3
            PRO  AY 120963-43-1
            SOL  7732-18-5 Water

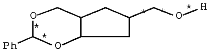
RX(23)      RCT  AY 120963-43-1
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BA 114179-59-8
            SOL  123-91-1 Dioxane

RX(25)      RCT  BA 114179-59-8, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BG 120963-46-4
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane

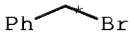

RX(229) OF 267 COMPOSED OF RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15),
            RX(17), RX(19), RX(21), RX(23), RX(25)
RX(229)     2 J  +  2 M  +  2 T  +  2 Y  +  AV  +  BF  ===>
            BG
```



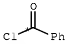
J



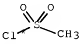
J



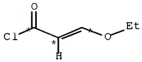
2 M



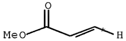
2 T



2 Y

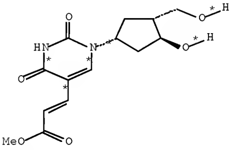


AV



BF

12
STEPS
→



BG
YIELD 72%

RX(4) RCT J 108275-94-1, M 100-39-0
RGT O 7693-26-7 KH
PRO N 120905-28-4
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4
RGT Q 7664-93-9 H2SO4
PRO P 120236-98-8
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4
RGT V 110-86-1 Pyridine
PRO U 120236-99-9
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0
RGT AA 121-44-8 Et3N
PRO Z 116142-70-2

```
          SOL   75-09-2 CH2Cl2

RX(11)    RCT   Z 116142-70-2
          RGT   AE 3396-11-0 Cs(OAc)2
          PRO   AC 120905-29-5, AD 120905-30-8
          SOL   67-68-5 DMSO

RX(13)    RCT   AC 120905-29-5
          RGT   AJ 1333-74-0 H2
          PRO   AI 120905-32-0
          CAT   7440-05-3 Pd
          SOL   64-17-5 EtOH

RX(15)    RCT   AI 120905-32-0
          RGT   AO 20039-37-6 PDC
          PRO   AN 120905-33-1
          SOL   68-12-2 DMF

RX(17)    RCT   AN 120905-33-1

            STAGE(1)
               RGT   AR 26386-88-9 (PhO)2P(O)N3
               SOL   71-43-2 Benzene

            STAGE(2)
               RGT   AS 7664-41-7 NH3

          PRO   AQ 120905-34-2

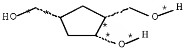
RX(19)    RCT   AQ 120905-34-2, AV 6191-99-7
          RGT   V 110-86-1 Pyridine
          PRO   AW 120905-35-3
          SOL   75-09-2 CH2Cl2

RX(21)    RCT   AW 120905-35-3
          RGT   AS 7664-41-7 NH3
          PRO   AY 120963-43-1
          SOL   7732-18-5 Water

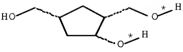
RX(23)    RCT   AY 120963-43-1
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BA 114179-59-8
          SOL   123-91-1 Dioxane

RX(25)    RCT   BA 114179-59-8, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BG 120963-46-4
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

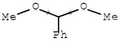

RX(230) OF 267 COMPOSED OF RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13),
          RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)
RX(230)   2 B  +  I  +  2 M  +  2 T  +  2 Y  +  AV  +  BF
          ===>  BG
```



B

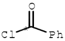


B

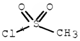


I

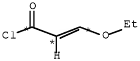
2 M



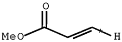
2 T



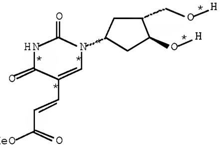
2 Y



AV



BF



BG
YIELD 72%

```
RX(3)     RCT  B 114129-19-0, I 1125-88-8
          RGT  K 16872-11-0 HBF4
          PRO  J 108275-94-1
          SOL  68-12-2 DMF

RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF
```

```
RX(5)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  P 120236-98-8
          SOL  7732-18-5 Water

RX(7)     RCT  P 120236-98-8, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2

RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

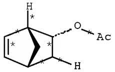
RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

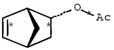
RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
```

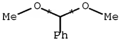
PRO BG 120963-46-4
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

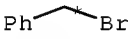
RX(231) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25)

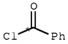
RX(231) 2 A + I + 2 M + 2 T + 2 Y + AV + BF
===> BG

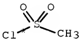

A

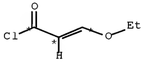

A

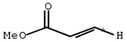

I


2 M

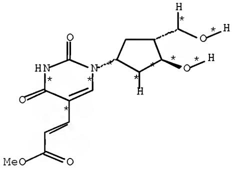

2 T


2 Y


AV


BF

14
STEPS
→


BG
YIELD 72%

RX(1) RCT A 112836-09-6

STAGE(1)
RGT C 10028-15-6 Ozone
SOL 67-56-1 MeOH

STAGE(2)

```
                RGT  D 16853-85-3 LiAlH4
                SOL  109-99-9 THF

           PRO  B 114129-19-0

RX(3)      RCT  B 114129-19-0, I 1125-88-8
           RGT  K 16872-11-0 HBF4
           PRO  J 108275-94-1
           SOL  68-12-2 DMF

RX(4)      RCT  J 108275-94-1, M 100-39-0
           RGT  O 7693-26-7 KH
           PRO  N 120905-28-4
           SOL  109-99-9 THF

RX(5)      RCT  N 120905-28-4
           RGT  Q 7664-93-9 H2SO4
           PRO  P 120236-98-8
           SOL  7732-18-5 Water

RX(7)      RCT  P 120236-98-8, T 98-88-4
           RGT  V 110-86-1 Pyridine
           PRO  U 120236-99-9
           SOL  75-09-2 CH2Cl2

RX(9)      RCT  U 120236-99-9, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  Z 116142-70-2
           SOL  75-09-2 CH2Cl2

RX(11)     RCT  Z 116142-70-2
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AC 120905-29-5, AD 120905-30-8
           SOL  67-68-5 DMSO

RX(13)     RCT  AC 120905-29-5
           RGT  AJ 1333-74-0 H2
           PRO  AI 120905-32-0
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(15)     RCT  AI 120905-32-0
           RGT  AO 20039-37-6 PDC
           PRO  AN 120905-33-1
           SOL  68-12-2 DMF

RX(17)     RCT  AN 120905-33-1

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
```

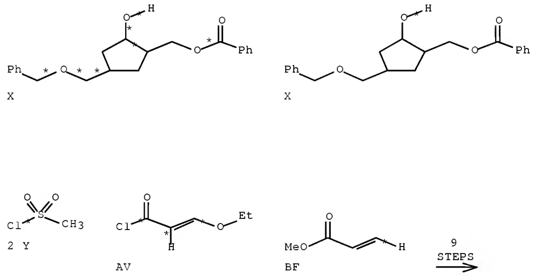
```
          SOL  75-09-2 CH2Cl2

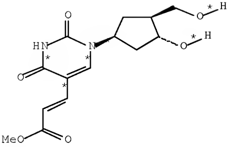
RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane


RX(232) OF 267 COMPOSED OF RX(10), RX(12), RX(14), RX(16), RX(18), RX(20),
          RX(22), RX(24), RX(26)
RX(232)   2 X  +  2 Y  +  AV  +  BF  ===>  BJ
```





BJ
YIELD 72%

```
RX(10)     RCT  X 120963-36-2, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  AB 120963-37-3
           SOL  75-09-2 CH2Cl2

RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

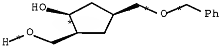
RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water
```

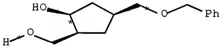
```
RX(24)      RCT  AZ 120963-44-2
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BE 120963-45-3
            SOL  123-91-1 Dioxane

RX(26)      RCT  BE 120963-45-3, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BJ 120963-47-5
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane

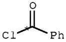

RX(233) OF 267 COMPOSED OF RX(8), RX(10), RX(12), RX(14), RX(16), RX(18),
            RX(20), RX(22), RX(24), RX(26)
RX(233)     2 S  +  2 T  +  2 Y  +  AV  +  BF  ===>
            BJ
```



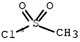
S



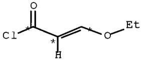
S



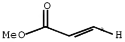
2 T



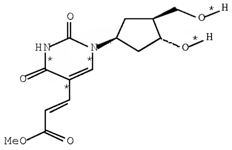
2 Y



AV



BF



BJ
YIELD 72%

```
RX(8)       RCT  S 120963-35-1, T 98-88-4
            RGT  V 110-86-1 Pyridine
            PRO  X 120963-36-2
            SOL  75-09-2 CH2Cl2

RX(10)      RCT  X 120963-36-2, Y 124-63-0
            RGT  AA 121-44-8 Et3N
            PRO  AB 120963-37-3
            SOL  75-09-2 CH2Cl2

RX(12)      RCT  AB 120963-37-3
            RGT  AE 3396-11-0 Cs(OAc)2
            PRO  AG 120963-38-4, AH 120905-31-9
            SOL  67-68-5 DMSO

RX(14)      RCT  AG 120963-38-4
            RGT  AJ 1333-74-0 H2
            PRO  AM 120963-39-5
            CAT  7440-05-3 Pd
            SOL  64-17-5 EtOH

RX(16)      RCT  AM 120963-39-5
            RGT  AO 20039-37-6 PDC
            PRO  AP 120963-40-8
            SOL  68-12-2 DMF

RX(18)      RCT  AP 120963-40-8

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AU 120963-41-9

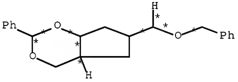
RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AX 120963-42-0
            SOL  75-09-2 CH2Cl2
```

```
RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

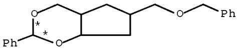
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

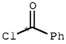

RX(234) OF 267 COMPOSED OF RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),
          RX(18), RX(20), RX(22), RX(24), RX(26)
RX(234)   2 N  +  2 T  +  2 Y  +  AV  +  BF  ===>
          BJ
```



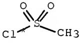
N



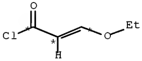
N



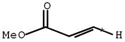
2 T



2 Y

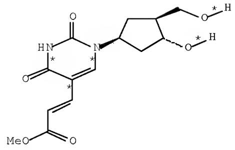


AV



BF

11
STEPS
⟶



BJ
YIELD 72%

```
RX(6)      RCT   N 120905-28-4
           RGT   Q 7664-93-9 H2SO4
           PRO   S 120963-35-1
           SOL   7732-18-5 Water

RX(8)      RCT   S 120963-35-1, T 98-88-4
           RGT   V 110-86-1 Pyridine
           PRO   X 120963-36-2
           SOL   75-09-2 CH2Cl2

RX(10)     RCT   X 120963-36-2, Y 124-63-0
           RGT   AA 121-44-8 Et3N
           PRO   AB 120963-37-3
           SOL   75-09-2 CH2Cl2

RX(12)     RCT   AB 120963-37-3
           RGT   AE 3396-11-0 Cs(OAc)2
           PRO   AG 120963-38-4, AH 120905-31-9
           SOL   67-68-5 DMSO

RX(14)     RCT   AG 120963-38-4
           RGT   AJ 1333-74-0 H2
           PRO   AM 120963-39-5
           CAT   7440-05-3 Pd
           SOL   64-17-5 EtOH

RX(16)     RCT   AM 120963-39-5
           RGT   AO 20039-37-6 PDC
           PRO   AP 120963-40-8
           SOL   68-12-2 DMF

RX(18)     RCT   AP 120963-40-8

             STAGE(1)
                RGT   AR 26386-88-9 (PhO)2P(O)N3
                SOL   71-43-2 Benzene

             STAGE(2)
                RGT   AS 7664-41-7 NH3

           PRO   AU 120963-41-9
```

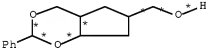
```
RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

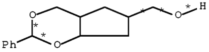
RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

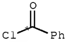
RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

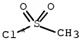

RX(235) OF 267 COMPOSED OF RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),
           RX(18), RX(20), RX(22), RX(24), RX(26)
RX(235)    2 J  +  2 M  +  2 T  +  2 Y  +  AV  +  BF  ===>
           BJ
```

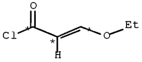

J

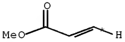

J

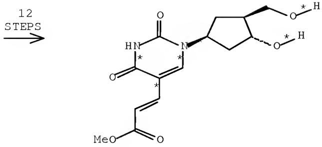

2 M


2 T


2 Y


AV


BF



BJ
YIELD 72%

```
RX(4)      RCT  J 108275-94-1, M 100-39-0
           RGT  O 7693-26-7 KH
           PRO  N 120905-28-4
           SOL  109-99-9 THF

RX(6)      RCT  N 120905-28-4
           RGT  Q 7664-93-9 H2SO4
           PRO  S 120963-35-1
           SOL  7732-18-5 Water

RX(8)      RCT  S 120963-35-1, T 98-88-4
           RGT  V 110-86-1 Pyridine
           PRO  X 120963-36-2
           SOL  75-09-2 CH2Cl2

RX(10)     RCT  X 120963-36-2, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  AB 120963-37-3
           SOL  75-09-2 CH2Cl2

RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT   AR 26386-88-9 (PhO)2P(O)N3
                SOL   71-43-2 Benzene
```

STAGE(2)
RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7
RGT V 110-86-1 Pyridine
PRO AX 120963-42-0
SOL 75-09-2 CH2Cl2

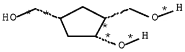
RX(22) RCT AX 120963-42-0
RGT AS 7664-41-7 NH3
PRO AZ 120963-44-2
SOL 7732-18-5 Water

RX(24) RCT AZ 120963-44-2
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3
PRO BE 120963-45-3
SOL 123-91-1 Dioxane

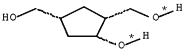
RX(26) RCT BE 120963-45-3, BF 96-33-3
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
PRO BJ 120963-47-5
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

RX(236) OF 267 COMPOSED OF RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26)

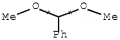
RX(236) 2 B + I + 2 M + 2 T + 2 Y + AV + BF
===> BJ



B

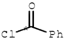


B

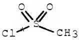


I

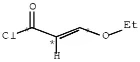
2 M



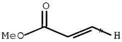
2 T



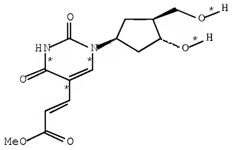
2 Y



AV



BF



BJ
YIELD 72%

```
RX(3)     RCT  B 114129-19-0, I 1125-88-8
          RGT  K 16872-11-0 HBF4
          PRO  J 108275-94-1
          SOL  68-12-2 DMF

RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF

RX(6)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  S 120963-35-1
          SOL  7732-18-5 Water

RX(8)     RCT  S 120963-35-1, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  X 120963-36-2
          SOL  75-09-2 CH2Cl2

RX(10)    RCT  X 120963-36-2, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  AB 120963-37-3
          SOL  75-09-2 CH2Cl2

RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO

RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
```

```
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

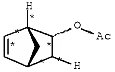
RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

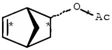
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

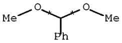

RX(237) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(6), RX(8), RX(10), RX(12),
          RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26)
RX(237)   2 A  +  I  +  2 M  +  2 T  +  2 Y  +  AV  +  BF
          ===>  BJ
```



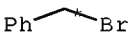
A



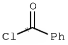
A

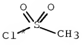


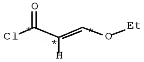
I

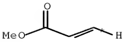


2 M

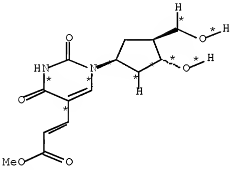

2 T


2 Y


AV


BF

14 STEPS
→


BJ
YIELD 72%

RX(1) RCT A 112836-09-6

STAGE(1)
RGT C 10028-15-6 Ozone
SOL 67-56-1 MeOH

STAGE(2)
RGT D 16853-85-3 LiAlH4
SOL 109-99-9 THF

PRO B 114129-19-0

RX(3) RCT B 114129-19-0, I 1125-88-8
RGT K 16872-11-0 HBF4
PRO J 108275-94-1
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0
RGT O 7693-26-7 KH
PRO N 120905-28-4
SOL 109-99-9 THF

RX(6) RCT N 120905-28-4
RGT Q 7664-93-9 H2SO4
PRO S 120963-35-1
SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4
RGT V 110-86-1 Pyridine

```
          PRO  X 120963-36-2
          SOL  75-09-2 CH2Cl2

RX(10)    RCT  X 120963-36-2, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  AB 120963-37-3
          SOL  75-09-2 CH2Cl2

RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO

RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

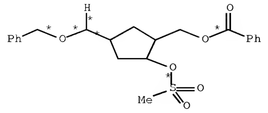
RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

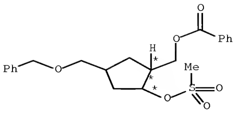
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

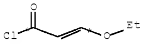

RX(238) OF 267 COMPOSED OF RX(11), RX(13), RX(15), RX(17), RX(19), RX(21),
          RX(23), RX(25), RX(27)
RX(238)   2 Z  +  AV  +  BF  ===>  BK
```



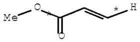
Z



Z

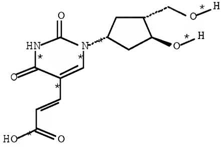


AV



BF

$\xrightarrow{\text{9 STEPS}}$



BK

```
RX(11)     RCT  Z 116142-70-2
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AC 120905-29-5, AD 120905-30-8
           SOL  67-68-5 DMSO

RX(13)     RCT  AC 120905-29-5
           RGT  AJ 1333-74-0 H2
           PRO  AI 120905-32-0
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(15)     RCT  AI 120905-32-0
           RGT  AO 20039-37-6 PDC
           PRO  AN 120905-33-1
           SOL  68-12-2 DMF
```

```
RX(17)     RCT  AN 120905-33-1

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AQ 120905-34-2

RX(19)     RCT  AQ 120905-34-2, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AW 120905-35-3
           SOL  75-09-2 CH2Cl2

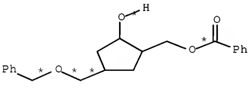
RX(21)     RCT  AW 120905-35-3
           RGT  AS 7664-41-7 NH3
           PRO  AY 120963-43-1
           SOL  7732-18-5 Water

RX(23)     RCT  AY 120963-43-1
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BA 114179-59-8
           SOL  123-91-1 Dioxane

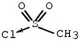
RX(25)     RCT  BA 114179-59-8, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BG 120963-46-4
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(27)     RCT  BG 120963-46-4
           RGT  BL 1310-58-3 KOH
           PRO  BK 120963-48-6

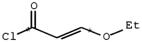

RX(239) OF 267 COMPOSED OF RX(9), RX(11), RX(13), RX(15), RX(17), RX(19),
           RX(21), RX(23), RX(25), RX(27)
RX(239)    U  +  Y  +  AV  +  BF  ===>  BK
```



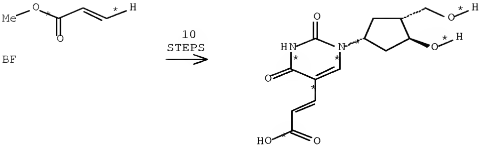
U



Y



AV



BF

BK

```
RX(9)       RCT  U 120236-99-9, Y 124-63-0
            RGT  AA 121-44-8 Et3N
            PRO  Z 116142-70-2
            SOL  75-09-2 CH2Cl2

RX(11)      RCT  Z 116142-70-2
            RGT  AE 3396-11-0 Cs(OAc)2
            PRO  AC 120905-29-5, AD 120905-30-8
            SOL  67-68-5 DMSO

RX(13)      RCT  AC 120905-29-5
            RGT  AJ 1333-74-0 H2
            PRO  AI 120905-32-0
            CAT  7440-05-3 Pd
            SOL  64-17-5 EtOH

RX(15)      RCT  AI 120905-32-0
            RGT  AO 20039-37-6 PDC
            PRO  AN 120905-33-1
            SOL  68-12-2 DMF

RX(17)      RCT  AN 120905-33-1

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AQ 120905-34-2

RX(19)      RCT  AQ 120905-34-2, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AW 120905-35-3
            SOL  75-09-2 CH2Cl2

RX(21)      RCT  AW 120905-35-3
            RGT  AS 7664-41-7 NH3
            PRO  AY 120963-43-1
            SOL  7732-18-5 Water

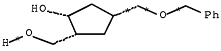
RX(23)      RCT  AY 120963-43-1
```

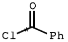
```
         RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
         PRO  BA 114179-59-8
         SOL  123-91-1 Dioxane

RX(25)   RCT  BA 114179-59-8, BF 96-33-3
         RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
         PRO  BG 120963-46-4
         CAT  3375-31-3 Pd(OAc)2
         SOL  123-91-1 Dioxane

RX(27)   RCT  BG 120963-46-4
         RGT  BL 1310-58-3 KOH
         PRO  BK 120963-48-6


RX(240) OF 267 COMPOSED OF RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),
         RX(19), RX(21), RX(23), RX(25), RX(27)
RX(240)   P  +  T  +  Y  +  AV  +  BF  ===>  BK
```


P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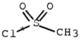
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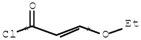
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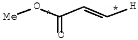
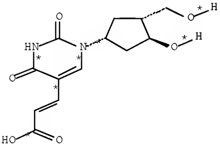

BF

11
STEPS


BK

```
RX(7)    RCT  P 120236-98-8, T 98-88-4
         RGT  V 110-86-1 Pyridine
         PRO  U 120236-99-9
```

```
         SOL  75-09-2 CH2Cl2

RX(9)    RCT  U 120236-99-9, Y 124-63-0
         RGT  AA 121-44-8 Et3N
         PRO  Z 116142-70-2
         SOL  75-09-2 CH2Cl2

RX(11)   RCT  Z 116142-70-2
         RGT  AE 3396-11-0 Cs(OAc)2
         PRO  AC 120905-29-5, AD 120905-30-8
         SOL  67-68-5 DMSO

RX(13)   RCT  AC 120905-29-5
         RGT  AJ 1333-74-0 H2
         PRO  AI 120905-32-0
         CAT  7440-05-3 Pd
         SOL  64-17-5 EtOH

RX(15)   RCT  AI 120905-32-0
         RGT  AO 20039-37-6 PDC
         PRO  AN 120905-33-1
         SOL  68-12-2 DMF

RX(17)   RCT  AN 120905-33-1

           STAGE(1)
              RGT  AR 26386-88-9 (PhO)2P(O)N3
              SOL  71-43-2 Benzene

           STAGE(2)
              RGT  AS 7664-41-7 NH3

         PRO  AQ 120905-34-2

RX(19)   RCT  AQ 120905-34-2, AV 6191-99-7
         RGT  V 110-86-1 Pyridine
         PRO  AW 120905-35-3
         SOL  75-09-2 CH2Cl2

RX(21)   RCT  AW 120905-35-3
         RGT  AS 7664-41-7 NH3
         PRO  AY 120963-43-1
         SOL  7732-18-5 Water

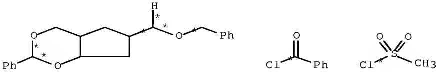
RX(23)   RCT  AY 120963-43-1
         RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
         PRO  BA 114179-59-8
         SOL  123-91-1 Dioxane

RX(25)   RCT  BA 114179-59-8, BF 96-33-3
         RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
         PRO  BG 120963-46-4
         CAT  3375-31-3 Pd(OAc)2
         SOL  123-91-1 Dioxane

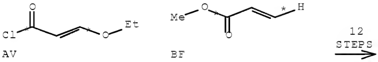
RX(27)   RCT  BG 120963-46-4
         RGT  BL 1310-58-3 KOH
         PRO  BK 120963-48-6
```

RX(241) OF 267 COMPOSED OF RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)

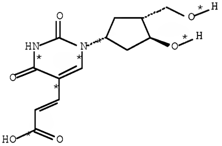
RX(241) N + T + Y + AV + BF ===> BK



N T Y



AV BF



BK

RX(5) RCT N 120905-28-4
RGT Q 7664-93-9 H2SO4
PRO P 120236-98-8
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4
RGT V 110-86-1 Pyridine
PRO U 120236-99-9
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0
RGT AA 121-44-8 Et3N
PRO Z 116142-70-2
SOL 75-09-2 CH2Cl2

RX(11) RCT Z 116142-70-2

```
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

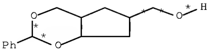
RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

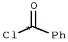
RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6


RX(242) OF 267 COMPOSED OF RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15),
          RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)
RX(242)   J  +  M  +  T  +  Y  +  AV  +  BF  ===>
          BK
```



J

M



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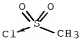
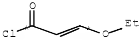
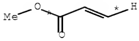


Y

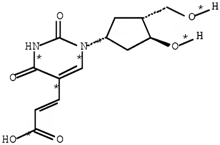


AV



BF

13 STEPS →



BK

```
RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF

RX(5)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  P 120236-98-8
          SOL  7732-18-5 Water

RX(7)     RCT  P 120236-98-8, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2

RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
```

```
            SOL  67-68-5 DMSO

RX(13)      RCT  AC 120905-29-5
            RGT  AJ 1333-74-0 H2
            PRO  AI 120905-32-0
            CAT  7440-05-3 Pd
            SOL  64-17-5 EtOH

RX(15)      RCT  AI 120905-32-0
            RGT  AO 20039-37-6 PDC
            PRO  AN 120905-33-1
            SOL  68-12-2 DMF

RX(17)      RCT  AN 120905-33-1

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AQ 120905-34-2

RX(19)      RCT  AQ 120905-34-2, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AW 120905-35-3
            SOL  75-09-2 CH2Cl2

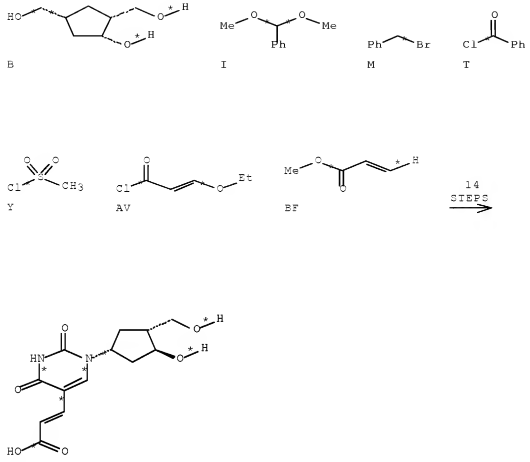
RX(21)      RCT  AW 120905-35-3
            RGT  AS 7664-41-7 NH3
            PRO  AY 120963-43-1
            SOL  7732-18-5 Water

RX(23)      RCT  AY 120963-43-1
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BA 114179-59-8
            SOL  123-91-1 Dioxane

RX(25)      RCT  BA 114179-59-8, BF 96-33-3
            RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
            PRO  BG 120963-46-4
            CAT  3375-31-3 Pd(OAc)2
            SOL  123-91-1 Dioxane

RX(27)      RCT  BG 120963-46-4
            RGT  BL 1310-58-3 KOH
            PRO  BK 120963-48-6


RX(243) OF 267 COMPOSED OF RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13),
            RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)
RX(243)     B  +  I  +  M  +  T  +  Y  +  AV  +  BF  ===>
            BK
```




```
RX(3)     RCT  B 114129-19-0, I 1125-88-8
          RGT  K 16872-11-0 HBF4
          PRO  J 108275-94-1
          SOL  68-12-2 DMF

RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF

RX(5)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  P 120236-98-8
          SOL  7732-18-5 Water

RX(7)     RCT  P 120236-98-8, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2

RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
```

```
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

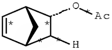
RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6


RX(244) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(5), RX(7), RX(9), RX(11),
          RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27)
RX(244)   A  +  I  +  M  +  T  +  Y  +  AV  +  BF  ===>
          BK
```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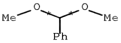
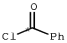

I


M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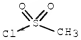
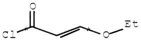
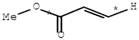
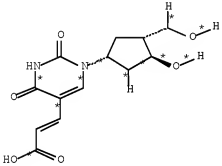

Y


AV


BF

15 STEPS →


BK

```
RX(1)     RCT  A 112836-09-6

            STAGE(1)
               RGT  C 10028-15-6 Ozone
               SOL  67-56-1 MeOH

            STAGE(2)
               RGT  D 16853-85-3 LiAlH4
               SOL  109-99-9 THF

          PRO  B 114129-19-0

RX(3)     RCT  B 114129-19-0, I 1125-88-8
          RGT  K 16872-11-0 HBF4
          PRO  J 108275-94-1
          SOL  68-12-2 DMF

RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF
```

```
RX(5)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  P 120236-98-8
          SOL  7732-18-5 Water

RX(7)     RCT  P 120236-98-8, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2

RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

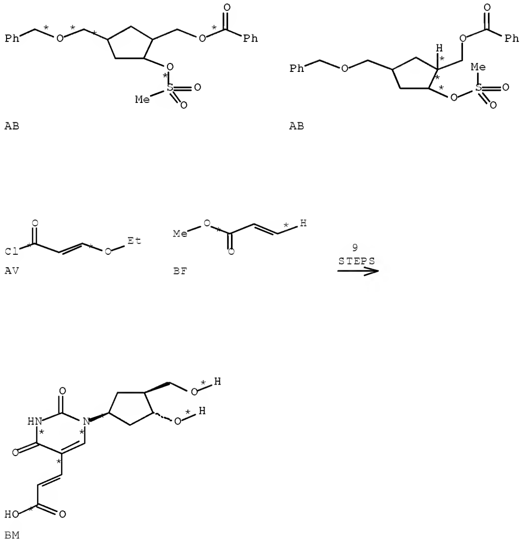
RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
```

```
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6


RX(245) OF 267 COMPOSED OF RX(12), RX(14), RX(16), RX(18), RX(20), RX(22),
          RX(24), RX(26), RX(28)
RX(245)   2 AB  +  AV  +  BF  ===>  BM
```




```
RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO
```

```
RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

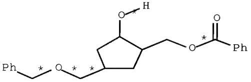
RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

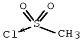
RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(28)     RCT  BJ 120963-47-5
           RGT  BL 1310-58-3 KOH
           PRO  BM 120963-49-7


RX(246) OF 267 COMPOSED OF RX(10), RX(12), RX(14), RX(16), RX(18), RX(20),
           RX(22), RX(24), RX(26), RX(28)
RX(246)    X  +  Y  +  AV  +  BF  ===>  BM
```



X



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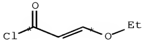
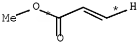
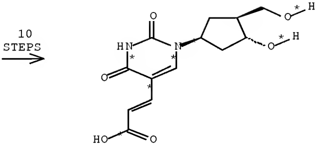


AV



BF



BM

```
RX(10)     RCT  X 120963-36-2, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  AB 120963-37-3
           SOL  75-09-2 CH2Cl2

RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3
```

```
          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

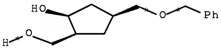
RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

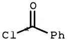
RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(28)    RCT  BJ 120963-47-5
          RGT  BL 1310-58-3 KOH
          PRO  BM 120963-49-7


RX(247) OF 267 COMPOSED OF RX(8), RX(10), RX(12), RX(14), RX(16), RX(18),
          RX(20), RX(22), RX(24), RX(26), RX(28)
RX(247)   S  +  T  +  Y  +  AV  +  BF  ===>  BM
```



S



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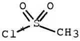

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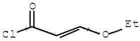

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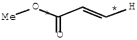
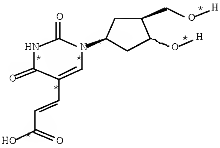


BF



BM

```
RX(8)       RCT  S 120963-35-1, T 98-88-4
            RGT  V 110-86-1 Pyridine
            PRO  X 120963-36-2
            SOL  75-09-2 CH2Cl2

RX(10)      RCT  X 120963-36-2, Y 124-63-0
            RGT  AA 121-44-8 Et3N
            PRO  AB 120963-37-3
            SOL  75-09-2 CH2Cl2

RX(12)      RCT  AB 120963-37-3
            RGT  AE 3396-11-0 Cs(OAc)2
            PRO  AG 120963-38-4, AH 120905-31-9
            SOL  67-68-5 DMSO

RX(14)      RCT  AG 120963-38-4
            RGT  AJ 1333-74-0 H2
            PRO  AM 120963-39-5
            CAT  7440-05-3 Pd
            SOL  64-17-5 EtOH

RX(16)      RCT  AM 120963-39-5
            RGT  AO 20039-37-6 PDC
            PRO  AP 120963-40-8
            SOL  68-12-2 DMF

RX(18)      RCT  AP 120963-40-8

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AU 120963-41-9

RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AX 120963-42-0
            SOL  75-09-2 CH2Cl2

RX(22)      RCT  AX 120963-42-0
```

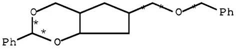
```
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(28)    RCT  BJ 120963-47-5
          RGT  BL 1310-58-3 KOH
          PRO  BM 120963-49-7


RX(248) OF 267 COMPOSED OF RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),
          RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)
RX(248)   N  +  T  +  Y  +  AV  +  BF  ===>  BM
```



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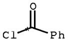

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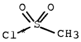

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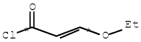

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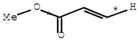
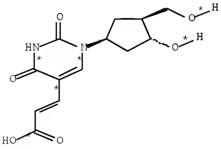


BF

12 STEPS →



BM

```
RX(6)       RCT  N 120905-28-4
            RGT  Q 7664-93-9 H2SO4
            PRO  S 120963-35-1
            SOL  7732-18-5 Water

RX(8)       RCT  S 120963-35-1, T 98-88-4
            RGT  V 110-86-1 Pyridine
            PRO  X 120963-36-2
            SOL  75-09-2 CH2Cl2

RX(10)      RCT  X 120963-36-2, Y 124-63-0
            RGT  AA 121-44-8 Et3N
            PRO  AB 120963-37-3
            SOL  75-09-2 CH2Cl2

RX(12)      RCT  AB 120963-37-3
            RGT  AE 3396-11-0 Cs(OAc)2
            PRO  AG 120963-38-4, AH 120905-31-9
            SOL  67-68-5 DMSO

RX(14)      RCT  AG 120963-38-4
            RGT  AJ 1333-74-0 H2
            PRO  AM 120963-39-5
            CAT  7440-05-3 Pd
            SOL  64-17-5 EtOH

RX(16)      RCT  AM 120963-39-5
            RGT  AO 20039-37-6 PDC
            PRO  AP 120963-40-8
            SOL  68-12-2 DMF

RX(18)      RCT  AP 120963-40-8

              STAGE(1)
                 RGT  AR 26386-88-9 (PhO)2P(O)N3
                 SOL  71-43-2 Benzene

              STAGE(2)
                 RGT  AS 7664-41-7 NH3

            PRO  AU 120963-41-9

RX(20)      RCT  AU 120963-41-9, AV 6191-99-7
            RGT  V 110-86-1 Pyridine
            PRO  AX 120963-42-0
            SOL  75-09-2 CH2Cl2

RX(22)      RCT  AX 120963-42-0
            RGT  AS 7664-41-7 NH3
            PRO  AZ 120963-44-2
            SOL  7732-18-5 Water

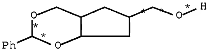
RX(24)      RCT  AZ 120963-44-2
            RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
            PRO  BE 120963-45-3
            SOL  123-91-1 Dioxane

RX(26)      RCT  BE 120963-45-3, BF 96-33-3
```

```
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BJ 120963-47-5
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

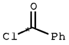
RX(28)    RCT   BJ 120963-47-5
          RGT   BL 1310-58-3 KOH
          PRO   BM 120963-49-7


RX(249) OF 267 COMPOSED OF RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),
          RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)
RX(249)   J  +  M  +  T  +  Y  +  AV  +  BF  ===>
          BM
```



J

M



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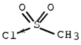

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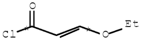

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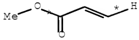

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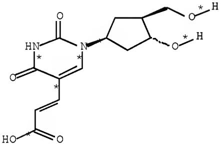


BM

```
RX(4)     RCT   J 108275-94-1, M 100-39-0
          RGT   O 7693-26-7 KH
          PRO   N 120905-28-4
          SOL   109-99-9 THF

RX(6)     RCT   N 120905-28-4
          RGT   Q 7664-93-9 H2SO4
```

```
          PRO   S 120963-35-1
          SOL   7732-18-5 Water

RX(8)     RCT   S 120963-35-1, T 98-88-4
          RGT   V 110-86-1 Pyridine
          PRO   X 120963-36-2
          SOL   75-09-2 CH2Cl2

RX(10)    RCT   X 120963-36-2, Y 124-63-0
          RGT   AA 121-44-8 Et3N
          PRO   AB 120963-37-3
          SOL   75-09-2 CH2Cl2

RX(12)    RCT   AB 120963-37-3
          RGT   AE 3396-11-0 Cs(OAc)2
          PRO   AG 120963-38-4, AH 120905-31-9
          SOL   67-68-5 DMSO

RX(14)    RCT   AG 120963-38-4
          RGT   AJ 1333-74-0 H2
          PRO   AM 120963-39-5
          CAT   7440-05-3 Pd
          SOL   64-17-5 EtOH

RX(16)    RCT   AM 120963-39-5
          RGT   AO 20039-37-6 PDC
          PRO   AP 120963-40-8
          SOL   68-12-2 DMF

RX(18)    RCT   AP 120963-40-8

            STAGE(1)
               RGT   AR 26386-88-9 (PhO)2P(O)N3
               SOL   71-43-2 Benzene

            STAGE(2)
               RGT   AS 7664-41-7 NH3

          PRO   AU 120963-41-9

RX(20)    RCT   AU 120963-41-9, AV 6191-99-7
          RGT   V 110-86-1 Pyridine
          PRO   AX 120963-42-0
          SOL   75-09-2 CH2Cl2

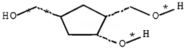
RX(22)    RCT   AX 120963-42-0
          RGT   AS 7664-41-7 NH3
          PRO   AZ 120963-44-2
          SOL   7732-18-5 Water

RX(24)    RCT   AZ 120963-44-2
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BE 120963-45-3
          SOL   123-91-1 Dioxane

RX(26)    RCT   BE 120963-45-3, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BJ 120963-47-5
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane
```

```
RX(28)      RCT  BJ 120963-47-5
            RGT  BL 1310-58-3 KOH
            PRO  BM 120963-49-7


RX(250) OF 267 COMPOSED OF RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14),
            RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)
RX(250)     B  +  I  +  M  +  T  +  Y  +  AV  +  BF  ===>
            BM
```



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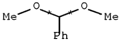

I

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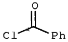

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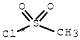
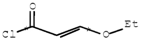
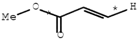


Y

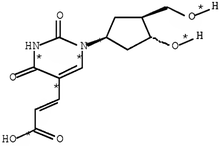


AV



BF

14 STEPS →



BM

```
RX(3)       RCT  B 114129-19-0, I 1125-88-8
            RGT  K 16872-11-0 HBF4
            PRO  J 108275-94-1
            SOL  68-12-2 DMF

RX(4)       RCT  J 108275-94-1, M 100-39-0
            RGT  O 7693-26-7 KH
            PRO  N 120905-28-4
            SOL  109-99-9 THF

RX(6)       RCT  N 120905-28-4
            RGT  Q 7664-93-9 H2SO4
```

```
          PRO  S 120963-35-1
          SOL  7732-18-5 Water

RX(8)     RCT  S 120963-35-1, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  X 120963-36-2
          SOL  75-09-2 CH2Cl2

RX(10)    RCT  X 120963-36-2, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  AB 120963-37-3
          SOL  75-09-2 CH2Cl2

RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO

RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

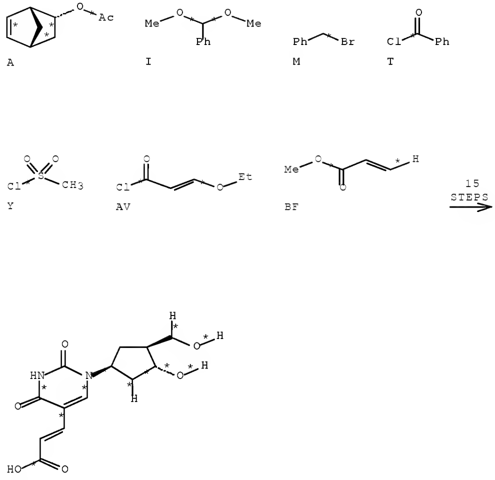
RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane
```

```
RX(28)      RCT  BJ 120963-47-5
            RGT  BL 1310-58-3 KOH
            PRO  BM 120963-49-7


RX(251) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(6), RX(8), RX(10), RX(12),
            RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28)
RX(251)     A  +  I  +  M  +  T  +  Y  +  AV  +  BF  ===>
            BM
```



BM

```
RX(1)       RCT  A 112836-09-6

              STAGE(1)
                 RGT  C 10028-15-6 Ozone
                 SOL  67-56-1 MeOH

              STAGE(2)
                 RGT  D 16853-85-3 LiAlH4
                 SOL  109-99-9 THF
```

```
          PRO  B 114129-19-0

RX(3)     RCT  B 114129-19-0, I 1125-88-8
          RGT  K 16872-11-0 HBF4
          PRO  J 108275-94-1
          SOL  68-12-2 DMF

RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF

RX(6)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  S 120963-35-1
          SOL  7732-18-5 Water

RX(8)     RCT  S 120963-35-1, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  X 120963-36-2
          SOL  75-09-2 CH2Cl2

RX(10)    RCT  X 120963-36-2, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  AB 120963-37-3
          SOL  75-09-2 CH2Cl2

RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO

RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
```

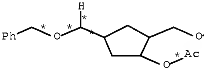
```
          RGT   AS 7664-41-7 NH3
          PRO   AZ 120963-44-2
          SOL   7732-18-5 Water

RX(24)    RCT   AZ 120963-44-2
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BE 120963-45-3
          SOL   123-91-1 Dioxane

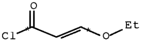
RX(26)    RCT   BE 120963-45-3, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BJ 120963-47-5
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

RX(28)    RCT   BJ 120963-47-5
          RGT   BL 1310-58-3 KOH
          PRO   BM 120963-49-7

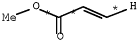

RX(252) OF 267 COMPOSED OF RX(13), RX(15), RX(17), RX(19), RX(21), RX(23),
          RX(25), RX(27), RX(29)
RX(252)   AC  +  AV  +  BF  ===>  BN
```



AC

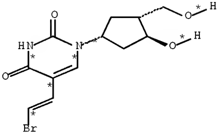


AV



BF

9 STEPS



BN

```
RX(13)    RCT   AC 120905-29-5
          RGT   AJ 1333-74-0 H2
          PRO   AI 120905-32-0
          CAT   7440-05-3 Pd
          SOL   64-17-5 EtOH

RX(15)    RCT   AI 120905-32-0
          RGT   AO 20039-37-6 PDC
```

```
          PRO   AN 120905-33-1
          SOL   68-12-2 DMF

RX(17)    RCT   AN 120905-33-1

            STAGE(1)
               RGT   AR 26386-88-9 (PhO)2P(O)N3
               SOL   71-43-2 Benzene

            STAGE(2)
               RGT   AS 7664-41-7 NH3

          PRO   AQ 120905-34-2

RX(19)    RCT   AQ 120905-34-2, AV 6191-99-7
          RGT   V 110-86-1 Pyridine
          PRO   AW 120905-35-3
          SOL   75-09-2 CH2Cl2

RX(21)    RCT   AW 120905-35-3
          RGT   AS 7664-41-7 NH3
          PRO   AY 120963-43-1
          SOL   7732-18-5 Water

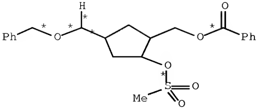
RX(23)    RCT   AY 120963-43-1
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BA 114179-59-8
          SOL   123-91-1 Dioxane

RX(25)    RCT   BA 114179-59-8, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BG 120963-46-4
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

RX(27)    RCT   BG 120963-46-4
          RGT   BL 1310-58-3 KOH
          PRO   BK 120963-48-6

RX(29)    RCT   BK 120963-48-6
          RGT   BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO   BN 95463-56-2
          SOL   68-12-2 DMF


RX(253) OF 267 COMPOSED OF RX(11), RX(13), RX(15), RX(17), RX(19), RX(21),
          RX(23), RX(25), RX(27), RX(29)
RX(253)   2 Z  +  AV  +  BF  ===>  BN
```



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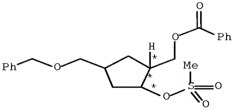

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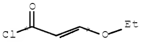
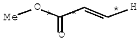
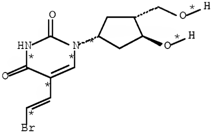


AV



BF

10 STEPS →



BN

```
RX(11)     RCT   Z 116142-70-2
           RGT   AE 3396-11-0 Cs(OAc)2
           PRO   AC 120905-29-5, AD 120905-30-8
           SOL   67-68-5 DMSO

RX(13)     RCT   AC 120905-29-5
           RGT   AJ 1333-74-0 H2
           PRO   AI 120905-32-0
           CAT   7440-05-3 Pd
           SOL   64-17-5 EtOH

RX(15)     RCT   AI 120905-32-0
           RGT   AO 20039-37-6 PDC
           PRO   AN 120905-33-1
           SOL   68-12-2 DMF

RX(17)     RCT   AN 120905-33-1

             STAGE(1)
```

```
              RGT  AR 26386-88-9 (PhO)2P(O)N3
              SOL  71-43-2 Benzene

           STAGE(2)
              RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

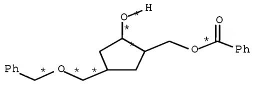
RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6

RX(29)    RCT  BK 120963-48-6
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BN 95463-56-2
          SOL  68-12-2 DMF


RX(254) OF 267 COMPOSED OF RX(9), RX(11), RX(13), RX(15), RX(17), RX(19),
          RX(21), RX(23), RX(25), RX(27), RX(29)
RX(254)   U  +  Y  +  AV  +  BF  ===>  BN
```



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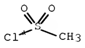

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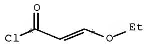
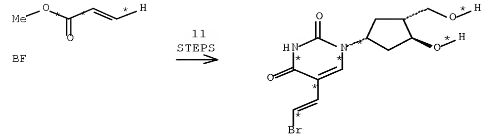


AV



BF

BN

```
RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
```

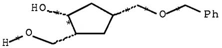
```
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

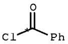
RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6

RX(29)    RCT  BK 120963-48-6
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BN 95463-56-2
          SOL  68-12-2 DMF


RX(255) OF 267 COMPOSED OF RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),
          RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)
RX(255)   P  +  T  +  Y  +  AV  +  BF  ===>  BN
```



P



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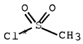

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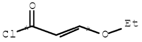
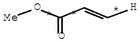
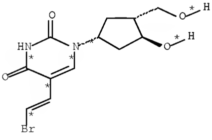


AV



BF

12 STEPS



BN

```
RX(7)     RCT  P 120236-98-8, T 98-88-4
```

```
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2

RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

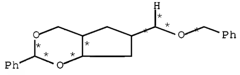
RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

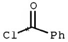
RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6
```

```
RX(29)      RCT  BK 120963-48-6
            RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
            PRO  BN 95463-56-2
            SOL  68-12-2 DMF


RX(256) OF 267 COMPOSED OF RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17),
            RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)
RX(256)     N  +  T  +  Y  +  AV  +  BF  ===>  BN
```



N



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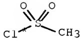
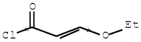
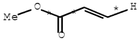


Y

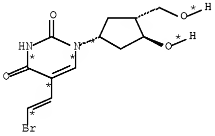


AV



BF

13 STEPS



BN

```
RX(5)       RCT  N 120905-28-4
            RGT  Q 7664-93-9 H2SO4
            PRO  P 120236-98-8
            SOL  7732-18-5 Water

RX(7)       RCT  P 120236-98-8, T 98-88-4
            RGT  V 110-86-1 Pyridine
            PRO  U 120236-99-9
            SOL  75-09-2 CH2Cl2

RX(9)       RCT  U 120236-99-9, Y 124-63-0
```

```
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
          RGT  AS 7664-41-7 NH3
          PRO  AY 120963-43-1
          SOL  7732-18-5 Water

RX(23)    RCT  AY 120963-43-1
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BA 114179-59-8
          SOL  123-91-1 Dioxane

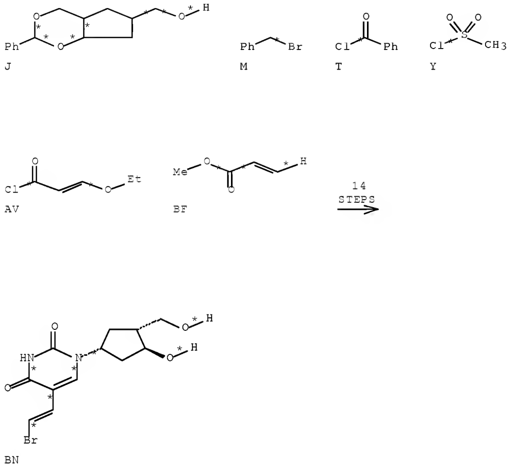
RX(25)    RCT  BA 114179-59-8, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BG 120963-46-4
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(27)    RCT  BG 120963-46-4
          RGT  BL 1310-58-3 KOH
          PRO  BK 120963-48-6

RX(29)    RCT  BK 120963-48-6
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BN 95463-56-2
          SOL  68-12-2 DMF
```

RX(257) OF 267 COMPOSED OF RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

RX(257) J + M + T + Y + AV + BF ===> BN



RX(4) RCT J 108275-94-1, M 100-39-0
RGT O 7693-26-7 KH
PRO N 120905-28-4
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4
RGT Q 7664-93-9 H2SO4
PRO P 120236-98-8
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4
RGT V 110-86-1 Pyridine
PRO U 120236-99-9
SOL 75-09-2 CH2Cl2

RX(9) RCT U 120236-99-9, Y 124-63-0
RGT AA 121-44-8 Et3N

```
         PRO  Z 116142-70-2
         SOL  75-09-2 CH2Cl2

RX(11)   RCT  Z 116142-70-2
         RGT  AE 3396-11-0 Cs(OAc)2
         PRO  AC 120905-29-5, AD 120905-30-8
         SOL  67-68-5 DMSO

RX(13)   RCT  AC 120905-29-5
         RGT  AJ 1333-74-0 H2
         PRO  AI 120905-32-0
         CAT  7440-05-3 Pd
         SOL  64-17-5 EtOH

RX(15)   RCT  AI 120905-32-0
         RGT  AO 20039-37-6 PDC
         PRO  AN 120905-33-1
         SOL  68-12-2 DMF

RX(17)   RCT  AN 120905-33-1

           STAGE(1)
              RGT  AR 26386-88-9 (PhO)2P(O)N3
              SOL  71-43-2 Benzene

           STAGE(2)
              RGT  AS 7664-41-7 NH3

         PRO  AQ 120905-34-2

RX(19)   RCT  AQ 120905-34-2, AV 6191-99-7
         RGT  V 110-86-1 Pyridine
         PRO  AW 120905-35-3
         SOL  75-09-2 CH2Cl2

RX(21)   RCT  AW 120905-35-3
         RGT  AS 7664-41-7 NH3
         PRO  AY 120963-43-1
         SOL  7732-18-5 Water

RX(23)   RCT  AY 120963-43-1
         RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
         PRO  BA 114179-59-8
         SOL  123-91-1 Dioxane

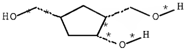
RX(25)   RCT  BA 114179-59-8, BF 96-33-3
         RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
         PRO  BG 120963-46-4
         CAT  3375-31-3 Pd(OAc)2
         SOL  123-91-1 Dioxane

RX(27)   RCT  BG 120963-46-4
         RGT  BL 1310-58-3 KOH
         PRO  BK 120963-48-6

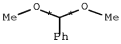
RX(29)   RCT  BK 120963-48-6
         RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
         PRO  BN 95463-56-2
         SOL  68-12-2 DMF
```

RX(258) OF 267 COMPOSED OF RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13),
RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

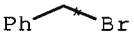
RX(258) B + I + M + T + Y + AV + BF ===>
BN



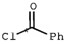
B



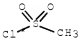
I



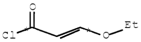
M



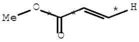
T



Y

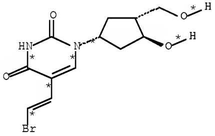


AV



BF

15 STEPS →



BN

RX(3) RCT B 114129-19-0, I 1125-88-8
RGT K 16872-11-0 HBF4
PRO J 108275-94-1
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0
RGT O 7693-26-7 KH
PRO N 120905-28-4
SOL 109-99-9 THF

RX(5) RCT N 120905-28-4
RGT Q 7664-93-9 H2SO4
PRO P 120236-98-8
SOL 7732-18-5 Water

RX(7) RCT P 120236-98-8, T 98-88-4
RGT V 110-86-1 Pyridine
PRO U 120236-99-9

```
         SOL  75-09-2 CH2Cl2

RX(9)    RCT  U 120236-99-9, Y 124-63-0
         RGT  AA 121-44-8 Et3N
         PRO  Z 116142-70-2
         SOL  75-09-2 CH2Cl2

RX(11)   RCT  Z 116142-70-2
         RGT  AE 3396-11-0 Cs(OAc)2
         PRO  AC 120905-29-5, AD 120905-30-8
         SOL  67-68-5 DMSO

RX(13)   RCT  AC 120905-29-5
         RGT  AJ 1333-74-0 H2
         PRO  AI 120905-32-0
         CAT  7440-05-3 Pd
         SOL  64-17-5 EtOH

RX(15)   RCT  AI 120905-32-0
         RGT  AO 20039-37-6 PDC
         PRO  AN 120905-33-1
         SOL  68-12-2 DMF

RX(17)   RCT  AN 120905-33-1

           STAGE(1)
              RGT  AR 26386-88-9 (PhO)2P(O)N3
              SOL  71-43-2 Benzene

           STAGE(2)
              RGT  AS 7664-41-7 NH3

         PRO  AQ 120905-34-2

RX(19)   RCT  AQ 120905-34-2, AV 6191-99-7
         RGT  V 110-86-1 Pyridine
         PRO  AW 120905-35-3
         SOL  75-09-2 CH2Cl2

RX(21)   RCT  AW 120905-35-3
         RGT  AS 7664-41-7 NH3
         PRO  AY 120963-43-1
         SOL  7732-18-5 Water

RX(23)   RCT  AY 120963-43-1
         RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
         PRO  BA 114179-59-8
         SOL  123-91-1 Dioxane

RX(25)   RCT  BA 114179-59-8, BF 96-33-3
         RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
         PRO  BG 120963-46-4
         CAT  3375-31-3 Pd(OAc)2
         SOL  123-91-1 Dioxane

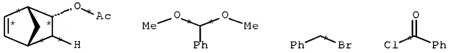
RX(27)   RCT  BG 120963-46-4
         RGT  BL 1310-58-3 KOH
         PRO  BK 120963-48-6

RX(29)   RCT  BK 120963-48-6
```

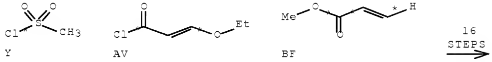
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
PRO BN 95463-56-2
SOL 68-12-2 DMF

RX(259) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(5), RX(7), RX(9), RX(11), RX(13), RX(15), RX(17), RX(19), RX(21), RX(23), RX(25), RX(27), RX(29)

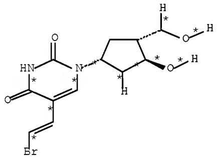
RX(259) A + I + M + T + Y + AV + BF ===> BN



A I M T



Y AV BF



BN

RX(1) RCT A 112836-09-6

STAGE(1)
RGT C 10028-15-6 Ozone
SOL 67-56-1 MeOH

STAGE(2)
RGT D 16853-85-3 LiAlH4
SOL 109-99-9 THF

```
          PRO  B 114129-19-0

RX(3)     RCT  B 114129-19-0, I 1125-88-8
          RGT  K 16872-11-0 HBF4
          PRO  J 108275-94-1
          SOL  68-12-2 DMF

RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF

RX(5)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  P 120236-98-8
          SOL  7732-18-5 Water

RX(7)     RCT  P 120236-98-8, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  U 120236-99-9
          SOL  75-09-2 CH2Cl2

RX(9)     RCT  U 120236-99-9, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  Z 116142-70-2
          SOL  75-09-2 CH2Cl2

RX(11)    RCT  Z 116142-70-2
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AC 120905-29-5, AD 120905-30-8
          SOL  67-68-5 DMSO

RX(13)    RCT  AC 120905-29-5
          RGT  AJ 1333-74-0 H2
          PRO  AI 120905-32-0
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(15)    RCT  AI 120905-32-0
          RGT  AO 20039-37-6 PDC
          PRO  AN 120905-33-1
          SOL  68-12-2 DMF

RX(17)    RCT  AN 120905-33-1

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AQ 120905-34-2

RX(19)    RCT  AQ 120905-34-2, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AW 120905-35-3
          SOL  75-09-2 CH2Cl2

RX(21)    RCT  AW 120905-35-3
```

```
          RGT   AS 7664-41-7 NH3
          PRO   AY 120963-43-1
          SOL   7732-18-5 Water

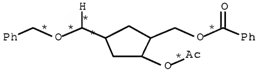
RX(23)    RCT   AY 120963-43-1
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BA 114179-59-8
          SOL   123-91-1 Dioxane

RX(25)    RCT   BA 114179-59-8, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BG 120963-46-4
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

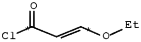
RX(27)    RCT   BG 120963-46-4
          RGT   BL 1310-58-3 KOH
          PRO   BK 120963-48-6

RX(29)    RCT   BK 120963-48-6
          RGT   BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO   BN 95463-56-2
          SOL   68-12-2 DMF

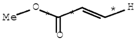

RX(260) OF 267 COMPOSED OF RX(14), RX(16), RX(18), RX(20), RX(22), RX(24),
          RX(26), RX(28), RX(30)
RX(260)   AG  +  AV  +  BF  ===>  BQ
```



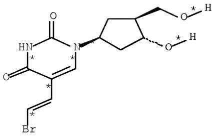
AG



AV



BF



BQ

```
RX(14)     RCT   AG 120963-38-4
           RGT   AJ 1333-74-0 H2
           PRO   AM 120963-39-5
           CAT   7440-05-3 Pd
           SOL   64-17-5 EtOH

RX(16)     RCT   AM 120963-39-5
           RGT   AO 20039-37-6 PDC
           PRO   AP 120963-40-8
           SOL   68-12-2 DMF

RX(18)     RCT   AP 120963-40-8

             STAGE(1)
                RGT   AR 26386-88-9 (PhO)2P(O)N3
                SOL   71-43-2 Benzene

             STAGE(2)
                RGT   AS 7664-41-7 NH3

           PRO   AU 120963-41-9

RX(20)     RCT   AU 120963-41-9, AV 6191-99-7
           RGT   V 110-86-1 Pyridine
           PRO   AX 120963-42-0
           SOL   75-09-2 CH2Cl2

RX(22)     RCT   AX 120963-42-0
           RGT   AS 7664-41-7 NH3
           PRO   AZ 120963-44-2
           SOL   7732-18-5 Water

RX(24)     RCT   AZ 120963-44-2
           RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO   BE 120963-45-3
           SOL   123-91-1 Dioxane

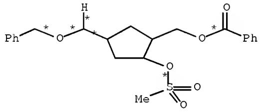
RX(26)     RCT   BE 120963-45-3, BF 96-33-3
           RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO   BJ 120963-47-5
           CAT   3375-31-3 Pd(OAc)2
           SOL   123-91-1 Dioxane

RX(28)     RCT   BJ 120963-47-5
```

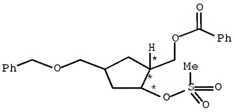
```
          RGT   BL 1310-58-3 KOH
          PRO   BM 120963-49-7

RX(30)    RCT   BM 120963-49-7
          RGT   BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO   BQ 120963-50-0
          SOL   68-12-2 DMF


RX(261) OF 267 COMPOSED OF RX(12), RX(14), RX(16), RX(18), RX(20), RX(22),
          RX(24), RX(26), RX(28), RX(30)
RX(261)   2 AB  +  AV  +  BF  ===>  BQ
```



AB



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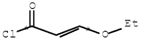

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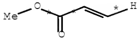
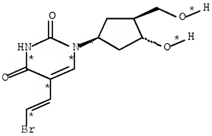


BF

10 STEPS →



BQ

```
RX(12)    RCT   AB 120963-37-3
          RGT   AE 3396-11-0 Cs(OAc)2
          PRO   AG 120963-38-4, AH 120905-31-9
          SOL   67-68-5 DMSO
```

```
RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

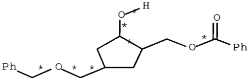
RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

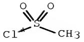
RX(28)     RCT  BJ 120963-47-5
           RGT  BL 1310-58-3 KOH
           PRO  BM 120963-49-7

RX(30)     RCT  BM 120963-49-7
           RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
           PRO  BQ 120963-50-0
           SOL  68-12-2 DMF

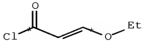

RX(262) OF 267 COMPOSED OF RX(10), RX(12), RX(14), RX(16), RX(18), RX(20),
           RX(22), RX(24), RX(26), RX(28), RX(30)
RX(262)    X  +  Y  +  AV  +  BF  ===>  BQ
```



X



Y



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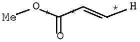
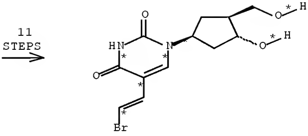


BF



BQ

RX(10)   RCT X 120963-36-2, Y 124-63-0
          RGT AA 121-44-8 Et3N
          PRO AB 120963-37-3
          SOL 75-09-2 CH2Cl2

RX(12)   RCT AB 120963-37-3
          RGT AE 3396-11-0 Cs(OAc)2
          PRO AG 120963-38-4, AH 120905-31-9
          SOL 67-68-5 DMSO

RX(14)   RCT AG 120963-38-4
          RGT AJ 1333-74-0 H2
          PRO AM 120963-39-5
          CAT 7440-05-3 Pd
          SOL 64-17-5 EtOH

RX(16)   RCT AM 120963-39-5
          RGT AO 20039-37-6 PDC
          PRO AP 120963-40-8
          SOL 68-12-2 DMF

RX(18)   RCT AP 120963-40-8

STAGE(1)
RGT AR 26386-88-9 (PhO)2P(O)N3
SOL 71-43-2 Benzene

STAGE(2)
RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

```
RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

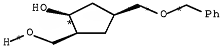
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

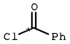
RX(28)    RCT  BJ 120963-47-5
          RGT  BL 1310-58-3 KOH
          PRO  BM 120963-49-7

RX(30)    RCT  BM 120963-49-7
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BQ 120963-50-0
          SOL  68-12-2 DMF


RX(263) OF 267 COMPOSED OF RX(8), RX(10), RX(12), RX(14), RX(16), RX(18),
          RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(263)   S  +  T  +  Y  +  AV  +  BF  ===>  BQ
```



S



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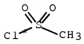
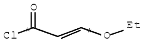
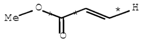


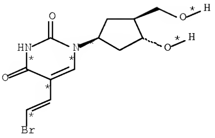
Y



AV



BF



BQ

```
RX(8)      RCT  S 120963-35-1, T 98-88-4
           RGT  V 110-86-1 Pyridine
           PRO  X 120963-36-2
           SOL  75-09-2 CH2Cl2

RX(10)     RCT  X 120963-36-2, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  AB 120963-37-3
           SOL  75-09-2 CH2Cl2

RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
```

```
          PRO   AZ 120963-44-2
          SOL   7732-18-5 Water

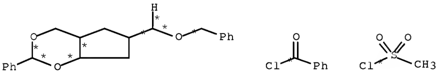
RX(24)    RCT   AZ 120963-44-2
          RGT   BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO   BE 120963-45-3
          SOL   123-91-1 Dioxane

RX(26)    RCT   BE 120963-45-3, BF 96-33-3
          RGT   BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO   BJ 120963-47-5
          CAT   3375-31-3 Pd(OAc)2
          SOL   123-91-1 Dioxane

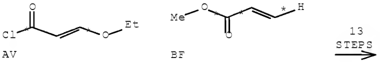
RX(28)    RCT   BJ 120963-47-5
          RGT   BL 1310-58-3 KOH
          PRO   BM 120963-49-7

RX(30)    RCT   BM 120963-49-7
          RGT   BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO   BQ 120963-50-0
          SOL   68-12-2 DMF

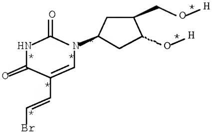

RX(264) OF 267 COMPOSED OF RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),
          RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(264)   N  +  T  +  Y  +  AV  +  BF  ===>  BQ
```



N T Y



AV BF



BQ

```
RX(6)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  S 120963-35-1
          SOL  7732-18-5 Water

RX(8)     RCT  S 120963-35-1, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  X 120963-36-2
          SOL  75-09-2 CH2Cl2

RX(10)    RCT  X 120963-36-2, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  AB 120963-37-3
          SOL  75-09-2 CH2Cl2

RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO

RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3

          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
```

PRO AX 120963-42-0
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0
RGT AS 7664-41-7 NH3
PRO AZ 120963-44-2
SOL 7732-18-5 Water

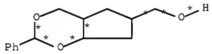
RX(24) RCT AZ 120963-44-2
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3
PRO BE 120963-45-3
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
PRO BJ 120963-47-5
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

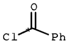
RX(28) RCT BJ 120963-47-5
RGT BL 1310-58-3 KOH
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
PRO BQ 120963-50-0
SOL 68-12-2 DMF

RX(265) OF 267 COMPOSED OF RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16),
RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(265) J + M + T + Y + AV + BF ===>
BQ


J


M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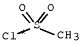
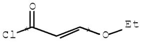

Y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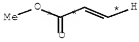
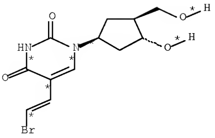

BF

14
STEPS



BQ

```
RX(4)     RCT  J 108275-94-1, M 100-39-0
          RGT  O 7693-26-7 KH
          PRO  N 120905-28-4
          SOL  109-99-9 THF

RX(6)     RCT  N 120905-28-4
          RGT  Q 7664-93-9 H2SO4
          PRO  S 120963-35-1
          SOL  7732-18-5 Water

RX(8)     RCT  S 120963-35-1, T 98-88-4
          RGT  V 110-86-1 Pyridine
          PRO  X 120963-36-2
          SOL  75-09-2 CH2Cl2

RX(10)    RCT  X 120963-36-2, Y 124-63-0
          RGT  AA 121-44-8 Et3N
          PRO  AB 120963-37-3
          SOL  75-09-2 CH2Cl2

RX(12)    RCT  AB 120963-37-3
          RGT  AE 3396-11-0 Cs(OAc)2
          PRO  AG 120963-38-4, AH 120905-31-9
          SOL  67-68-5 DMSO

RX(14)    RCT  AG 120963-38-4
          RGT  AJ 1333-74-0 H2
          PRO  AM 120963-39-5
          CAT  7440-05-3 Pd
          SOL  64-17-5 EtOH

RX(16)    RCT  AM 120963-39-5
          RGT  AO 20039-37-6 PDC
          PRO  AP 120963-40-8
          SOL  68-12-2 DMF

RX(18)    RCT  AP 120963-40-8

            STAGE(1)
               RGT  AR 26386-88-9 (PhO)2P(O)N3
               SOL  71-43-2 Benzene

            STAGE(2)
               RGT  AS 7664-41-7 NH3
```

```
          PRO  AU 120963-41-9

RX(20)    RCT  AU 120963-41-9, AV 6191-99-7
          RGT  V 110-86-1 Pyridine
          PRO  AX 120963-42-0
          SOL  75-09-2 CH2Cl2

RX(22)    RCT  AX 120963-42-0
          RGT  AS 7664-41-7 NH3
          PRO  AZ 120963-44-2
          SOL  7732-18-5 Water

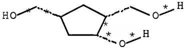
RX(24)    RCT  AZ 120963-44-2
          RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
          PRO  BE 120963-45-3
          SOL  123-91-1 Dioxane

RX(26)    RCT  BE 120963-45-3, BF 96-33-3
          RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
          PRO  BJ 120963-47-5
          CAT  3375-31-3 Pd(OAc)2
          SOL  123-91-1 Dioxane

RX(28)    RCT  BJ 120963-47-5
          RGT  BL 1310-58-3 KOH
          PRO  BM 120963-49-7

RX(30)    RCT  BM 120963-49-7
          RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
          PRO  BQ 120963-50-0
          SOL  68-12-2 DMF


RX(266) OF 267 COMPOSED OF RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14),
          RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(266)   B  +  I  +  M  +  T  +  Y  +  AV  +  BF  ===>
          BQ
```



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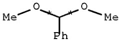

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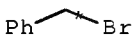
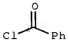


M



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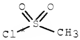

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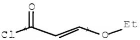
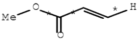


AV



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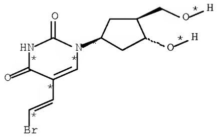


BQ

```
RX(3)      RCT  B 114129-19-0, I 1125-88-8
           RGT  K 16872-11-0 HBF4
           PRO  J 108275-94-1
           SOL  68-12-2 DMF

RX(4)      RCT  J 108275-94-1, M 100-39-0
           RGT  O 7693-26-7 KH
           PRO  N 120905-28-4
           SOL  109-99-9 THF

RX(6)      RCT  N 120905-28-4
           RGT  Q 7664-93-9 H2SO4
           PRO  S 120963-35-1
           SOL  7732-18-5 Water

RX(8)      RCT  S 120963-35-1, T 98-88-4
           RGT  V 110-86-1 Pyridine
           PRO  X 120963-36-2
           SOL  75-09-2 CH2Cl2

RX(10)     RCT  X 120963-36-2, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  AB 120963-37-3
           SOL  75-09-2 CH2Cl2

RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
```

RGT AR 26386-88-9 (PhO)2P(O)N3
SOL 71-43-2 Benzene

STAGE(2)
RGT AS 7664-41-7 NH3

PRO AU 120963-41-9

RX(20) RCT AU 120963-41-9, AV 6191-99-7
RGT V 110-86-1 Pyridine
PRO AX 120963-42-0
SOL 75-09-2 CH2Cl2

RX(22) RCT AX 120963-42-0
RGT AS 7664-41-7 NH3
PRO AZ 120963-44-2
SOL 7732-18-5 Water

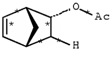
RX(24) RCT AZ 120963-44-2
RGT BB 7553-56-2 I2, BC 7697-37-2 HNO3
PRO BE 120963-45-3
SOL 123-91-1 Dioxane

RX(26) RCT BE 120963-45-3, BF 96-33-3
RGT BH 603-35-0 PPh3, AA 121-44-8 Et3N
PRO BJ 120963-47-5
CAT 3375-31-3 Pd(OAc)2
SOL 123-91-1 Dioxane

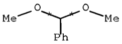
RX(28) RCT BJ 120963-47-5
RGT BL 1310-58-3 KOH
PRO BM 120963-49-7

RX(30) RCT BM 120963-49-7
RGT BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
PRO BQ 120963-50-0
SOL 68-12-2 DMF

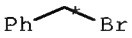
RX(267) OF 267 COMPOSED OF RX(1), RX(3), RX(4), RX(6), RX(8), RX(10), RX(12), RX(14), RX(16), RX(18), RX(20), RX(22), RX(24), RX(26), RX(28), RX(30)
RX(267) A + I + M + T + Y + AV + BF ===>
BQ



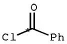
A



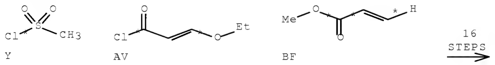
I



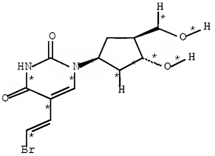
M



T



Y AV BF



BQ

RX(1) RCT A 112836-09-6

STAGE(1)
RGT C 10028-15-6 Ozone
SOL 67-56-1 MeOH

STAGE(2)
RGT D 16853-85-3 LiAlH4
SOL 109-99-9 THF

PRO B 114129-19-0

RX(3) RCT B 114129-19-0, I 1125-88-8
RGT K 16872-11-0 HBF4
PRO J 108275-94-1
SOL 68-12-2 DMF

RX(4) RCT J 108275-94-1, M 100-39-0
RGT O 7693-26-7 KH
PRO N 120905-28-4
SOL 109-99-9 THF

RX(6) RCT N 120905-28-4
RGT Q 7664-93-9 H2SO4
PRO S 120963-35-1
SOL 7732-18-5 Water

RX(8) RCT S 120963-35-1, T 98-88-4
RGT V 110-86-1 Pyridine
PRO X 120963-36-2
SOL 75-09-2 CH2Cl2

```
RX(10)     RCT  X 120963-36-2, Y 124-63-0
           RGT  AA 121-44-8 Et3N
           PRO  AB 120963-37-3
           SOL  75-09-2 CH2Cl2

RX(12)     RCT  AB 120963-37-3
           RGT  AE 3396-11-0 Cs(OAc)2
           PRO  AG 120963-38-4, AH 120905-31-9
           SOL  67-68-5 DMSO

RX(14)     RCT  AG 120963-38-4
           RGT  AJ 1333-74-0 H2
           PRO  AM 120963-39-5
           CAT  7440-05-3 Pd
           SOL  64-17-5 EtOH

RX(16)     RCT  AM 120963-39-5
           RGT  AO 20039-37-6 PDC
           PRO  AP 120963-40-8
           SOL  68-12-2 DMF

RX(18)     RCT  AP 120963-40-8

             STAGE(1)
                RGT  AR 26386-88-9 (PhO)2P(O)N3
                SOL  71-43-2 Benzene

             STAGE(2)
                RGT  AS 7664-41-7 NH3

           PRO  AU 120963-41-9

RX(20)     RCT  AU 120963-41-9, AV 6191-99-7
           RGT  V 110-86-1 Pyridine
           PRO  AX 120963-42-0
           SOL  75-09-2 CH2Cl2

RX(22)     RCT  AX 120963-42-0
           RGT  AS 7664-41-7 NH3
           PRO  AZ 120963-44-2
           SOL  7732-18-5 Water

RX(24)     RCT  AZ 120963-44-2
           RGT  BB 7553-56-2 I2, BC 7697-37-2 HNO3
           PRO  BE 120963-45-3
           SOL  123-91-1 Dioxane

RX(26)     RCT  BE 120963-45-3, BF 96-33-3
           RGT  BH 603-35-0 PPh3, AA 121-44-8 Et3N
           PRO  BJ 120963-47-5
           CAT  3375-31-3 Pd(OAc)2
           SOL  123-91-1 Dioxane

RX(28)     RCT  BJ 120963-47-5
           RGT  BL 1310-58-3 KOH
           PRO  BM 120963-49-7

RX(30)     RCT  BM 120963-49-7
           RGT  BO 298-14-6 KHCO3, BP 128-08-5 Bromosuccinimide
           PRO  BQ 120963-50-0
```

SOL 68-12-2 DMF

L46 ANSWER 18 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 107:40117 CASREACT Full-text

TITLE: Stereoselective synthesis of (±)-cis-α-irone

AUTHOR(S): Nussbaumer, Cornelius; Frater, Georg

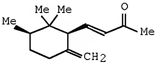
CORPORATE SOURCE: Givaudan Forschungsges. A.-G., Duebendorf, CH-8600, Switz.

SOURCE: Journal of Organic Chemistry (1987), 52(10), 2096-8 CODEN: JOCEAH; ISSN: 0022-3263

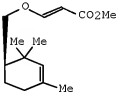
DOCUMENT TYPE: Journal

LANGUAGE: English

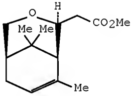
GI



I



II

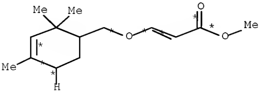


III

AB (±)-cis-Irone (I) was stereoselectively synthesized in 36% overall yield in 7 steps from (2,2,4-trimethyl-3-cyclohexen-1-yl)methanol via a β-alkoxyacrylate-olefin cyclization of II to III as the key step.

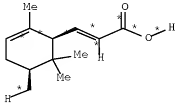
RX(24) OF 28 COMPOSED OF RX(3), RX(4), RX(5), RX(6), RX(7)

RX(24) G ===> A



G

5 STEPS →



A
YIELD 76%

RX(3) RCT G 107890-58-4
RGT K 67-56-1 MeOH
PRO J 107890-60-8
SOL 75-09-2 CH2Cl2

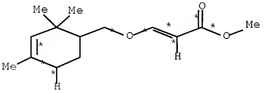
RX(4) RCT J 107890-60-8
RGT N 1310-73-2 NaOH
PRO M 107890-61-9
SOL 67-56-1 MeOH, 7732-18-5 Water

RX(5) RCT M 107890-61-9
RGT Q 4111-54-0 LiN(Pr-i)2
PRO P 107890-62-0
SOL 109-99-9 THF, 110-54-3 Hexane

RX(6) RCT P 107890-62-0
RGT U 124-63-0 MeSO2Cl
PRO T 107890-63-1
SOL 75-09-2 CH2Cl2, 110-86-1 Pyridine

RX(7) RCT T 107890-63-1
RGT W 7681-82-5 NaI, X 7440-66-6 Zn
PRO A 107890-64-2
SOL 110-71-4 (CH2OMe)2

RX(27) OF 28 COMPOSED OF RX(3), RX(4), RX(5), RX(6), RX(7), RX(1)
RX(27) G + B ===> C

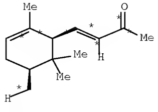


G

H3C—Li

B

6 STEPS ⟶



C
YIELD 89%

```
RX(3)     RCT  G 107890-58-4
          RGT  K 67-56-1 MeOH
          PRO  J 107890-60-8
          SOL  75-09-2 CH2Cl2

RX(4)     RCT  J 107890-60-8
          RGT  N 1310-73-2 NaOH
          PRO  M 107890-61-9
          SOL  67-56-1 MeOH, 7732-18-5 Water

RX(5)     RCT  M 107890-61-9
          RGT  Q 4111-54-0 LiN(Pr-i)2
          PRO  P 107890-62-0
          SOL  109-99-9 THF, 110-54-3 Hexane

RX(6)     RCT  P 107890-62-0
          RGT  U 124-63-0 MeSO2Cl
          PRO  T 107890-63-1
          SOL  75-09-2 CH2Cl2, 110-86-1 Pyridine

RX(7)     RCT  T 107890-63-1
          RGT  W 7681-82-5 NaI, X 7440-66-6 Zn
          PRO  A 107890-64-2
          SOL  110-71-4 (CH2OMe)2

RX(1)     RCT  A 107890-64-2, B 917-54-4
          PRO  C 472-46-8
          SOL  60-29-7 Et2O
```

L46 ANSWER 19 OF 24 CASREACT

ACCESSION NUMBER: 99:53063 CASREACT Full-text

TITLE: 3-Alkoxyacroleins: malonic dialdehyde equivalents

AUTHOR(S): Maddaluno, Jacques; D'Angelo, Jean

CORPORATE SOURCE: Lab. Chim. Org. Synth., Univ. Pierre et Marie Curie, Paris, 75005, Fr.

SOURCE: Tetrahedron Letters (1983), 24(9), 895-8
CODEN: TELEAY; ISSN: 0040-4039

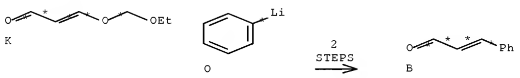
DOCUMENT TYPE: Journal

LANGUAGE: French

AB (E)-ROCH:CHCHO (I; R = Me, MeOCH2, EtOCH2, PhCH2OCH2), useful as synthetic equivs. of malondialdehyde, were prepared in 80% yield by alkylation of NaOCH:CHCHO with MeO3SF, MeOCH2Cl, EtOCH2Cl, and PhCH2OCH2Cl, resp., at room temperature for 12 h. Some synthetic applications of I are described. E.g., treatment of I with organolithiums gave α-substituted allylic alcs. which were

hydrolyzed by acids to give β-substituted acroleins. Thus, I (R = EtOCH2) with PhLi cong. NH4Cl at -78° for 10 min gave (E)-EtOCH2OCH:CHCHPhOH which was hydrolyzed by acid to give HCOCH:CHPh.

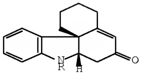
RX(15) OF 18 COMPOSED OF RX(7), RX(1)
RX(15) K + O ===> B

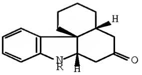


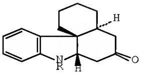
RX(7) RCT K 86557-99-5, O 591-51-5
PRO A 86558-09-0

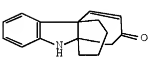
RX(1) RCT A 86558-09-0
RGT C 7647-01-0 HCl
PRO B 104-55-2

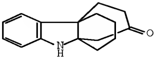
L46 ANSWER 20 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 95:203164 CASREACT Full-text
TITLE: Rearrangement of N-acetylacetaldehyde derivatives of indoles. Part 5. Di- and tetrahydro derivatives of rearrangement products of 4-(tetrahydrocarbazol-9-yl)-3-buten-2-one
AUTHOR(S): Teuber, Hans Joachim; Gholami, Abbas; Reinehr, Ulrich; Paulus, Erich
CORPORATE SOURCE: Inst. Org. Chem., Univ. Frankfurt, Frankfurt/Main, D-6000/50, Fed. Rep. Ger.
SOURCE: Liebigs Annalen der Chemie (1981), (4), 569-80
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: German
GI


I


II

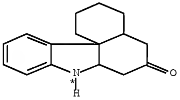

III

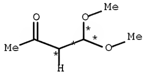

IV


V

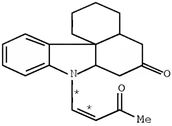
AB Catalytic hydrogenation of I (R = H, CH:CHCOMe) gave II and III (same R), the configurations of which were assigned by x-ray anal. The relative configurations of the chiral centers in III (R = H) were determined, and the cyclohexanone ring was shown to have the boat conformation. NaBH4 reduction of I (R = H) and III occurred stereoselectively to give the corresponding alcs. with axial and equatorial OH groups, resp. Both the configuration and the conformation of these alcs. could be determined from IR and NMR spectra. NaBH4 reduction of II (R = H), IV, and V gave epimeric mixts. of alcs.

RX(5) OF 12 ...B + H ===> G


B


H

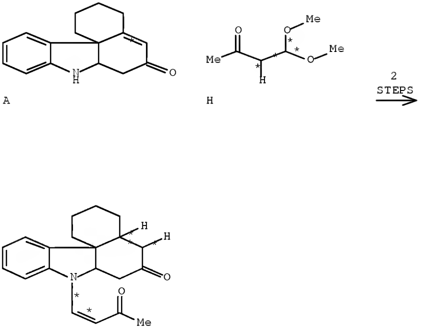
$\xrightarrow{(5)}$



G
YIELD 54%

```
RX(5)       RCT  B 72181-49-8, H 5436-21-5
            RGT  I 7647-01-0 HCl
            PRO  G 72181-58-9

RX(10) OF 12 COMPOSED OF RX(1), RX(5)
RX(10)      A  +  H  ===>  G
```



G
YIELD 54%

```
RX(1)       RCT  A 2398-19-8
            PRO  B 72181-49-8
            CAT  7727-43-7 BaSO4

RX(5)       RCT  B 72181-49-8, H 5436-21-5
            RGT  I 7647-01-0 HCl
```

PRO G 72181-58-9

L46 ANSWER 21 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 92:58534 CASREACT Full-text

TITLE: Rearrangement of 4-(tetrahydrocarbazol-9-yl)- and 4-(tetrahydrocyclopent[b]indol-4-yl)-3-buten-2-one

AUTHOR(S): Teuber, Hans Joachim; Gholami, Abbas; Reinehr, Ulrich; Bader, Hans Joachim

CORPORATE SOURCE: Inst. Org. Chem., Univ. Frankfurt, Frankfurt/Main, D-6000/50, Fed. Rep. Ger.

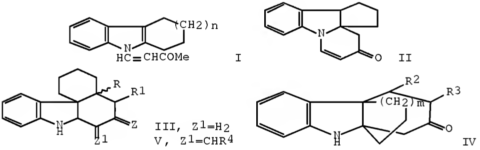
SOURCE: Liebigs Annalen der Chemie (1979), (7), 1048-66

CODEN: LACHDL; ISSN: 0170-2041

DOCUMENT TYPE: Journal

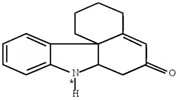
LANGUAGE: German

GI

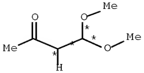


AB Cycloalkanoindoles I (n = 0, 1) reacted in HCl-MeOH to give, besides the cyclization product II, the rearrangement products ketones III (RR1 = bond, Z = O) and IV (R2R3 = bond, m = 1, 2) with propellane structure. II and IV (R2R3 = bond, m = 2) as well as IV (R2R3 = bond, m = 1) and III (RR1 = bond, Z = O) are in equilibrium III (RR1 = bond, Z = O) was hydrogenated to III (R = R1 = H, Z = O), which was isolated in 2 stereoisomeric forms corresponding to cis- and trans-decalone. The N-benzoyl derivative of II (R = R1 = H, Z = H2), formed by hydrogenation, has the same structure as the appropriately modified product obtained by Fischer cyclization from trans-α-decalone. III (RR1 = bond, Z = O) and IV (R2R3 = bond, m = 1, 2), as well as the corresponding saturated ketones III (R = R1 = H, Z = O) and IV (R2 = R3 = H, m = 1, 2) were converted into derivs. by reaction at the oxo and amino functions. III (RR1 = bond, Z = O) and BzH with Na-EtOH gave the benzylidene derivative V (RR1 = bond, R4 = Ph).

RX(4) OF 67 ...E + I ===> J...

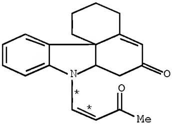


E



I

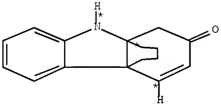
(4)



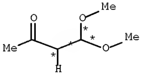
J
YIELD 63%

RX(4)   RCT E 2398-19-8, I 5436-21-5
           RGT F 7647-01-0 HCl
           PRO J 2398-25-6

RX(5) OF 67   ...H + I ===> J...

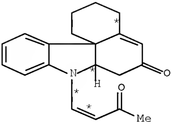


H



I

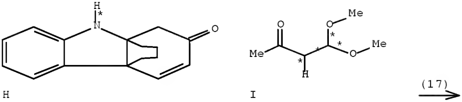
(5)



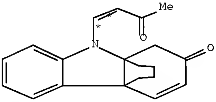
J
YIELD 78%

```
RX(5)      RCT  H 69393-74-4, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  J 2398-25-6
```

RX(17) OF 67   ...H + I ===> AF



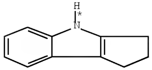
H   I

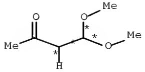


AF
YIELD 54%

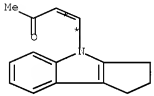
```
RX(17)     RCT  H 69393-74-4, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  AF 72181-69-2
```

RX(22) OF 67   ...B + I ===> K...


B

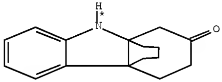

I

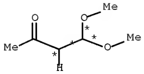
(22) →


K
YIELD 40%

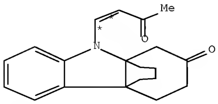
RX(22) RCT B 2047-91-8, I 5436-21-5
RGT F 7647-01-0 HCl
PRO K 69393-75-5

RX(25) OF 67 ...AG + I ===> AN


AG

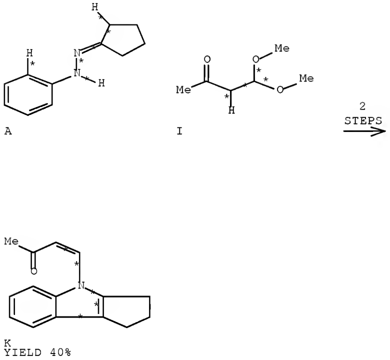

I

(25) →


AN
YIELD 63%

```
RX(25)      RCT  AG 72181-70-5, I 5436-21-5
            RGT  F 7647-01-0 HCl
            PRO  AN 72181-73-8

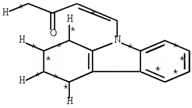

RX(26) OF 67 COMPOSED OF RX(1), RX(22)
RX(26)      A  +  I  ===>  K
```



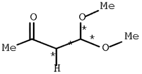
```
RX(1)       RCT  A 1132-58-7
            RGT  C 7664-93-9 H2SO4
            PRO  B 2047-91-8

RX(22)      RCT  B 2047-91-8, I 5436-21-5
            RGT  F 7647-01-0 HCl
            PRO  K 69393-75-5


RX(28) OF 67 COMPOSED OF RX(2), RX(4)
RX(28)      D  +  I  ===>  J
```

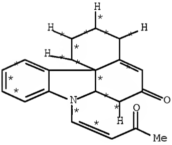


D



I

2 STEPS →

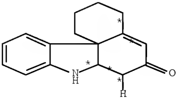


J
YIELD 63%

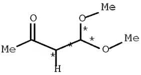
```
RX(2)      RCT   D 2646-01-7
           RGT   F 7647-01-0 HCl
           PRO   E 2398-19-8
           SOL   67-56-1 MeOH

RX(4)      RCT   E 2398-19-8, I 5436-21-5
           RGT   F 7647-01-0 HCl
           PRO   J 2398-25-6


RX(36) OF 67 COMPOSED OF RX(3), RX(5)
RX(36)     E  +  I  ===>  J
```

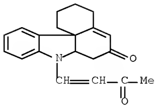


E



I

2 STEPS →

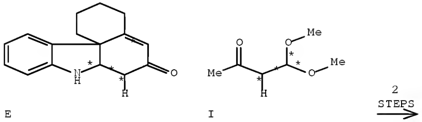


J
YIELD 78%

```
RX(3)      RCT  E 2398-19-8
           RGT  F 7647-01-0 HCl
           PRO  H 69393-74-4
           SOL  67-56-1 MeOH

RX(5)      RCT  H 69393-74-4, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  J 2398-25-6

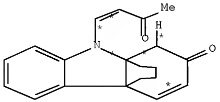

RX(37) OF 67 COMPOSED OF RX(3), RX(17)
RX(37)     E  +  I  ===>  AF
```



E

I

2 STEPS



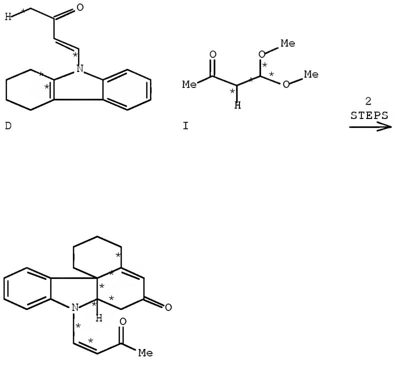
AF
YIELD 54%

```
RX(3)      RCT  E 2398-19-8
```

RGT F 7647-01-0 HCl
PRO H 69393-74-4
SOL 67-56-1 MeOH

RX(17) RCT H 69393-74-4, I 5436-21-5
RGT F 7647-01-0 HCl
PRO AF 72181-69-2

RX(39) OF 67 COMPOSED OF RX(21), RX(5)
RX(39) D + I ===> J



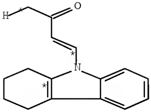
D I

J
YIELD 78%

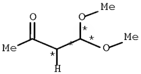
RX(21) RCT D 2646-01-7
RGT F 7647-01-0 HCl
PRO H 69393-74-4
SOL 67-56-1 MeOH

RX(5) RCT H 69393-74-4, I 5436-21-5
RGT F 7647-01-0 HCl
PRO J 2398-25-6

RX(40) OF 67 COMPOSED OF RX(21), RX(17)
RX(40) D + I ===> AF

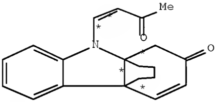


D



I

2
STEPS

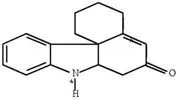


AF
YIELD 54%

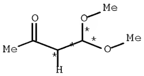
RX(21)   RCT   D 2646-01-7
           RGT   F 7647-01-0 HCl
           PRO   H 69393-74-4
           SOL   67-56-1 MeOH

RX(17)   RCT   H 69393-74-4, I 5436-21-5
           RGT   F 7647-01-0 HCl
           PRO   AF 72181-69-2

RX(42) OF 67 COMPOSED OF RX(4), RX(12)
RX(42)   E + I ===> Y

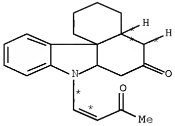


E



I

2
STEPS

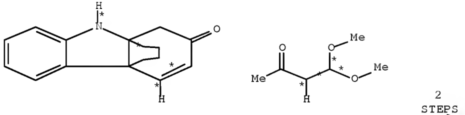


Y
YIELD 47%

```
RX(4)       RCT  E 2398-19-8, I 5436-21-5
            RGT  F 7647-01-0 HCl
            PRO  J 2398-25-6

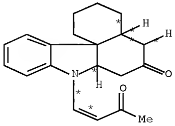
RX(12)      RCT  J 2398-25-6
            RGT  X 7727-43-7 BaSO4
            PRO  Y 72181-58-9


RX(43) OF 67 COMPOSED OF RX(5), RX(12)
RX(43)      H  +  I  ===>  Y
```



H

I



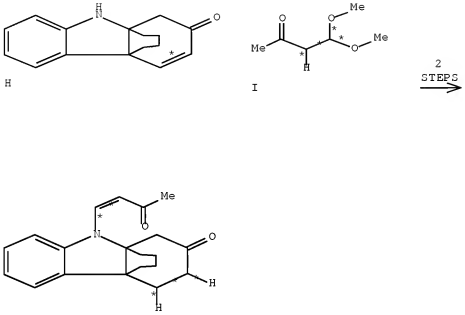
Y
YIELD 47%

```
RX(5)       RCT  H 69393-74-4, I 5436-21-5
            RGT  F 7647-01-0 HCl
```

```
          PRO   J 2398-25-6

RX(12)    RCT   J 2398-25-6
          RGT   X 7727-43-7 BaSO4
          PRO   Y 72181-58-9


RX(48) OF 67 COMPOSED OF RX(18), RX(25)
RX(48)    H  +  I  ===>  AN
```

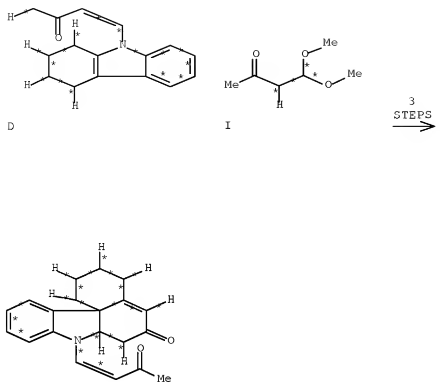


AN
YIELD 63%

```
RX(18)    RCT   H 69393-74-4
          RGT   X 7727-43-7 BaSO4
          PRO   AG 72181-70-5

RX(25)    RCT   AG 72181-70-5, I 5436-21-5
          RGT   F 7647-01-0 HCl
          PRO   AN 72181-73-8


RX(53) OF 67 COMPOSED OF RX(2), RX(3), RX(5)
RX(53)    D  +  I  ===>  J
```



D

I

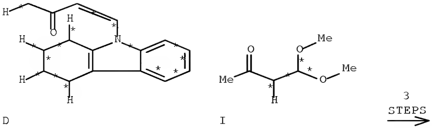
J
YIELD 78%

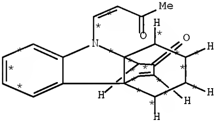
RX(2) RCT D 2646-01-7
RGT F 7647-01-0 HCl
PRO E 2398-19-8
SOL 67-56-1 MeOH

RX(3) RCT E 2398-19-8
RGT F 7647-01-0 HCl
PRO H 69393-74-4
SOL 67-56-1 MeOH

RX(5) RCT H 69393-74-4, I 5436-21-5
RGT F 7647-01-0 HCl
PRO J 2398-25-6

RX(54) OF 67 COMPOSED OF RX(2), RX(3), RX(17)
RX(54) D + I ===> AF





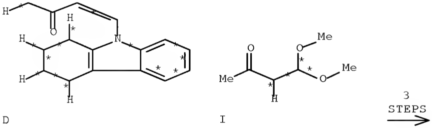
AF
YIELD 54%

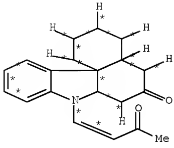
RX(2)   RCT D 2646-01-7
           RGT F 7647-01-0 HCl
           PRO E 2398-19-8
           SOL 67-56-1 MeOH

RX(3)   RCT E 2398-19-8
           RGT F 7647-01-0 HCl
           PRO H 69393-74-4
           SOL 67-56-1 MeOH

RX(17)   RCT H 69393-74-4, I 5436-21-5
           RGT F 7647-01-0 HCl
           PRO AF 72181-69-2

RX(56) OF 67 COMPOSED OF RX(2), RX(4), RX(12)
RX(56)   D + I ===> Y





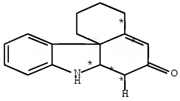
Y
YIELD 47%

RX(2)   RCT D 2646-01-7
           RGT F 7647-01-0 HCl
           PRO E 2398-19-8
           SOL 67-56-1 MeOH

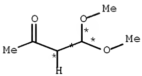
RX(4)   RCT E 2398-19-8, I 5436-21-5
           RGT F 7647-01-0 HCl
           PRO J 2398-25-6

RX(12)   RCT J 2398-25-6
           RGT X 7727-43-7 BaSO4
           PRO Y 72181-58-9

RX(60) OF 67 COMPOSED OF RX(3), RX(5), RX(12)
RX(60)   E + I ===> Y

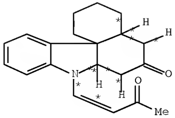


E



I

3
STEPS



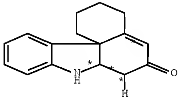
Y
YIELD 47%

```
RX(3)      RCT  E 2398-19-8
           RGT  F 7647-01-0 HCl
           PRO  H 69393-74-4
           SOL  67-56-1 MeOH

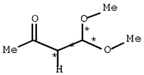
RX(5)      RCT  H 69393-74-4, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  J 2398-25-6

RX(12)     RCT  J 2398-25-6
           RGT  X 7727-43-7 BaSO4
           PRO  Y 72181-58-9

RX(61) OF 67 COMPOSED OF RX(3), RX(18), RX(25)
RX(61)     E  +  I  ===>  AN
```

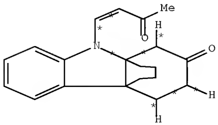


E



I

3 STEPS →



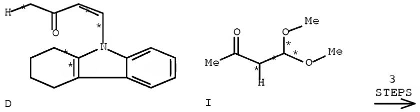
AN
YIELD 63%

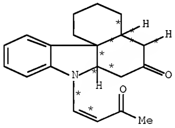
```
RX(3)      RCT  E 2398-19-8
           RGT  F 7647-01-0 HCl
           PRO  H 69393-74-4
           SOL  67-56-1 MeOH

RX(18)     RCT  H 69393-74-4
           RGT  X 7727-43-7 BaSO4
           PRO  AG 72181-70-5

RX(25)     RCT  AG 72181-70-5, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  AN 72181-73-8


RX(62) OF 67 COMPOSED OF RX(21), RX(5), RX(12)
RX(62)     D  +  I  ===>  Y
```





Y
YIELD 47%

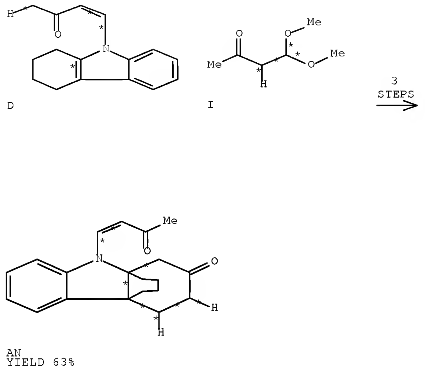
```
RX(21)     RCT  D 2646-01-7
           RGT  F 7647-01-0 HCl
           PRO  H 69393-74-4
           SOL  67-56-1 MeOH

RX(5)      RCT  H 69393-74-4, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  J 2398-25-6

RX(12)     RCT  J 2398-25-6
```

RGT X 7727-43-7 BaSO4
PRO Y 72181-58-9

RX(63) OF 67 COMPOSED OF RX(21), RX(18), RX(25)
RX(63) D + I ===> AN



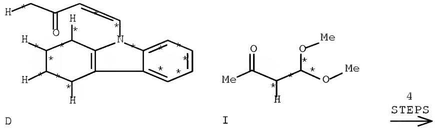
YIELD 63%

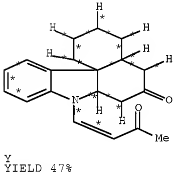
RX(21) RCT D 2646-01-7
RGT F 7647-01-0 HCl
PRO H 69393-74-4
SOL 67-56-1 MeOH

RX(18) RCT H 69393-74-4
RGT X 7727-43-7 BaSO4
PRO AG 72181-70-5

RX(25) RCT AG 72181-70-5, I 5436-21-5
RGT F 7647-01-0 HCl
PRO AN 72181-73-8

RX(64) OF 67 COMPOSED OF RX(2), RX(3), RX(5), RX(12)
RX(64) D + I ===> Y





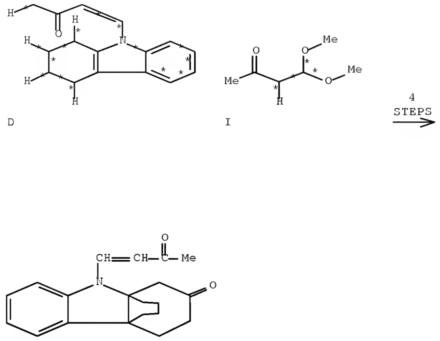

```
RX(2)      RCT  D 2646-01-7
           RGT  F 7647-01-0 HCl
           PRO  E 2398-19-8
           SOL  67-56-1 MeOH

RX(3)      RCT  E 2398-19-8
           RGT  F 7647-01-0 HCl
           PRO  H 69393-74-4
           SOL  67-56-1 MeOH

RX(5)      RCT  H 69393-74-4, I 5436-21-5
           RGT  F 7647-01-0 HCl
           PRO  J 2398-25-6

RX(12)     RCT  J 2398-25-6
           RGT  X 7727-43-7 BaSO4
           PRO  Y 72181-58-9

RX(65) OF 67 COMPOSED OF RX(2), RX(3), RX(18), RX(25)
RX(65)     D  +  I  ===>  AN
```



AN
YIELD 63%

```
RX(2)     RCT  D 2646-01-7
          RGT  F 7647-01-0 HCl
          PRO  E 2398-19-8
          SOL  67-56-1 MeOH

RX(3)     RCT  E 2398-19-8
          RGT  F 7647-01-0 HCl
          PRO  H 69393-74-4
          SOL  67-56-1 MeOH

RX(18)    RCT  H 69393-74-4
          RGT  X 7727-43-7 BaSO4
          PRO  AG 72181-70-5

RX(25)    RCT  AG 72181-70-5, I 5436-21-5
          RGT  F 7647-01-0 HCl
          PRO  AN 72181-73-8
```

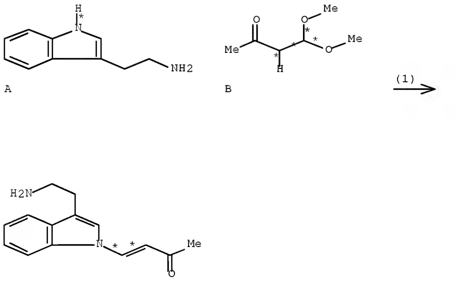
L46 ANSWER 22 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	60:52625 CASREACT Full-text
TITLE:	Syntheses of heterocycles with hydroxymethylene ketones. IV. A new condensation product from tryptamine and acetoacetaldehyde
AUTHOR(S):	Teuber, Hans Joachim; Glosauer, Otto; Hochmuth, Udo
CORPORATE SOURCE:	Univ. Frankfurt, Germany
SOURCE:	Chemische Berichte (1964), 97(2), 557-62 CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. CA 58, 13905c; 59, 15247e. Tryptamine-HCl (I.HCl) with a small amount concentrated HCl and AcCH2CH(OMe)2 (II) yielded 70% III.HCl, m. 193-4° (decomposition). I and II in dilute H2SO4 heated 0.5 hr. at 70-80° gave 1,3,5-C6H3Ac3 (IV), needles, m. 161-3° (80% EtOH), and a yellow oil which in MeOH with aqueous KNCO yielded the urea derivative (V) of I, prisms, m. 204-7° (decomposition) III.HCl with 2N NaOH gave about 30% yellow-brown prisms, III, decompose 103-7° (1:1 Me2CO-C6H6), which changed during several months to a viscous brown resin; III gave a deep red color in concentrated H2SO4; picrate m. 202-6° (EtOH); urea derivative, prisms, decompose 206-8° (MeOH); phenylurea derivs., prisms, decomposing 220-2° (EtOH); N-Ac derivative, needles, m. 154-5° (hot H2O); 2,4-dinitrophenylhydrazone, dark red prisms, m. above 260°; oxime, pale yellow needles, decompose 196-8° (EtOH). III.HCl in absolute MeOH treated 2 days at 20° with saturated HClMeOH and then with 10% NaOH gave I, decomposing 145-6°; I.HCl, m. 244-6° (EtOH). The attempted reduction of III.HCl with NaBH4 in 90% EtOH gave only an unidentified crystalline product, pale yellow in concentrated H2SO4. III.HCl and methylal in AcOH refluxed 24 hrs. yielded about 80% tetrahydronorharman- HCl.0.5H2O (VI.HCl.0.5H2O), decompose 254-6° with a color change to red-brown; picrate m. 244-9° (decomposition). VI.HCl with aqueous NaHCO3 yielded VI, m. 203-5° (C6H6), and IV, m. 162-3°. The ultraviolet absorption spectrum of I.HCl is recorded.

RX(1) OF 2 A + B ===> C



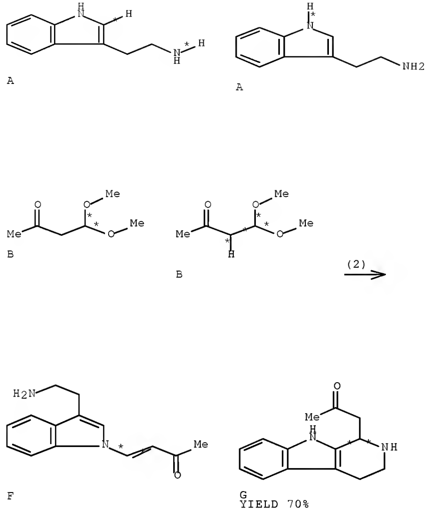
A B

C
YIELD 70%

```
RX(1)     RCT  A 61-54-1, B 5436-21-5
          RGT  D 7647-01-0 HCl
          PRO  C 92255-25-9
          SOL  7732-18-5 Water
          NTE  Classification: Elimination; N-Alkylation; # Conditions:
               MeCOCH2CH(OMe)2; HCl 5-10mn; # Comments: reactant and product
```

are chloride salts

RX(2) OF 2   2 A + 2 B ===> F + G



RX(2)   RCT A 61-54-1, B 5436-21-5
          RGT D 7647-01-0 HCl
          PRO F 157103-25-8, G 69225-88-3
          NTE Classification: Heterocycle formation; Condensation; N-Alkylation; Elimination; # Conditions: HCl 5-10mn; # Comments: Pictet-Spengler reaction; reactant and product as hydrochloride salts; tricyclic minor product

L46 ANSWER 23 OF 24 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 59:82171 CASREACT Full-text
TITLE: N-Substitution of indoles with hydroxymethylene ketones
AUTHOR(S):   Teuber, Hans Joachim; Cornelius, Dieter; Pfaff, Herbert

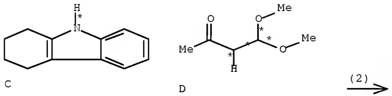
CORPORATE SOURCE: Univ. Frankfurt, Germany
SOURCE: Chemische Berichte (1963), 96(10), 2617-31
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

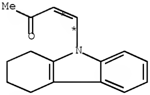
AB Indoles with protected 2- and 2,3-positions react with AcCH2H(OEt)2 (I) and EtOCH:CHCH(OEt)2 (II) in the presence of concentrated HCl to yield the corresponding 1-AcCH:CH and I-OHCCH:CH derivs., which are reduced by NaBH4 to acid-sensitive dihydro derivs. with an allyl alc. function, and over Raney Ni to tetrahydro derivs. with a saturated 1-substituent. The combination of condensation and reduction constitutes a simple method for the N-alkylation of indoles. Skatole reacted beyond the 1-substituted derivative Dihydroindoles, such as 5-acetylindoline (III) and hexahydrocarbazole (IV), react in the same manner as the indoles, but the condensation products differ, because of the greater basicity of the N, from the corresponding compds. in the indole series in their reactive and spectroscopic behavior. The course of the condensation reaction and its relations to alkaloid chemistry are discussed. 1,2,3,4-Tetrahydrocarbazole (V) (5 g.) in 10 cc. I stirred 17-18 min. with 2 cc. concentrated HCl, diluted with H2O, and filtered, and the residue recrystd. from 30 cc. EtOH yielded 6 g. AcCH:CH derivative (VI) of V, ivory-colored rods and prisms, m. 127-9°; it is cleaved by 12N HCl even at 20°. VI (480 mg.) and 280 mg. NH2OH.HCl in 15 cc. C5H5N kept overnight and diluted with H2O gave the oxime, decomposing 191-2° (EtOH). VI (480 mg.) in 20 cc. C5H5N kept overnight with 480 mg. H2NCONHNH2.HCl in 1 cc. H2O gave the semicarbazone, needles, m. 183-5° (MeOH). VI (360 mg.) in 50 cc. MeOH kept overnight with 360 mg. NaBH4, diluted with H2O, and extracted with Et2O gave the N-MeCH(OH)CH:CH derivative (VII) of V, m. 85-6° (ligroine, b. 50-80°). VI (240 mg.) in 20 cc. MeOH hydrogenated 5 hrs. over Raney Ni gave the NMeCH(OH)CH2CH2 derivative (VIII) of V, m. 80-2° (ligroine). 1-Me derivative (1.85 g.) of V, 4 cc. I, and 1 cc. concentrated HCl yielded in the usual manner the 1-Me derivative of N-(3-oxo-l-butenyl)-1,2,3,4-tetrahydrocarbazole (IX), ivory-colored crystals, m. 118° (EtOH); oxime m. 177-8° (decomposition) (EtOH). V (1.7 g.) in 5 cc. II treated with 5 drops concentrated HCl and diluted after 2-3 min. with H2O gave 70 80% N-OHCCH:CH derivative (X) of V, orange needles,re. 132°(EtOH). X(225mg.)and 140mg. NH2OH.HCl in 10 cc. C5H5N gave during 5 hrs. the oxime, pale yellow needles, m.) 158°. 1-OH derivative (560 mg.) of V, 2 cc. I, and 10 drops concentrated HCl gave octahydro[1,9:9',1']bicarbazolylene, m. 275-8° (C6H6). Carbazole (XI) (5.0 g.), 10 cc. I, and 2 cc. concentrated HCl stirred 15 min. and diluted with H2O yielded 6.3 g. N-AcCH:CH derivative (XII) of XI, m. 138-9° (EtOH). XII (235 mg.) in 50 cc. 12N HCl diluted after 1 hr. with H2O gave XI. XII (350 mg.) treated overnight with 210 mg. NH2OH.HCl in 10 cc. C5H5N yielded the oxime, m. 176 7° (decomposition) (EtOH). XII (350 mg.) in 50 cc. MeOH treated overnight with 350 mg. NaBH4 yielded N-(3-hydroxy-1-butenyl)carbazole (XIII), needles, m. 104-5°. XI (1.7 g.), 3 cc. II, 2 cc. EtOH, and 3 drops concentrated HCl stirred about 3 min. yielded 900 mg. N-OHCCH:CH derivative (XIV) of XI, pale yellow needles, m. 156° (EtOH). XIV (220 mg.), 140 mg. NH2OH.HCl, and 10 cc. C5H5N kept overnight yielded the oxime, m. 164 7° (EtOH). XIV (330 mg.) in 50 cc. MeOH kept overnight with NaBH4 gave a mixture of N-HOCH2CH:CH derivative (XV) of XI and XI, m. 200-5°, with sintering at 120-5°. 1-Hydroxycarbazole (XVI) (1.85 g.), m. 158°, in 4 cc. I and 1 cc. concentrated HCl stirred 15 min. and diluted with H2O gave over 90% N-AcCH:CH derivative (XVII) of XVI, m. 203-4° (EtOH). A similar run with com. 2-hydroxycarbazole (apparently containing XVI) gave after standing overnight a dark resin; this, powdered, dissolved in Me2CO, filtered through Al2O3, and evapd, gave XIII, m. 205-6° (EtOH); further elution of the column with MeOH, evaporation of the eluate, and chromatography of the residue again on Al2O3 gave a blue solid, C32H28N2O5, m. 150-6°, after sintering from 90°.

2,3-Dimethylindole (1.45 g.), 3 cc. I, and 0.5 cc. concentrated HCl stirred 15 min. and diluted with H2O yielded over 95% 1-AcCH:CH derivative (XVIII), pale yellow crystals, m. 110° (aqueous EtOH). XVIII (320 mg.) with 210 mg. NH2OH.HCl in 10 cc. C5H5N gave overnight the oxime, m. 171-4° (decomposition) (EtOH). Skatole (3.9 g.) in 10 cc. I stirred 0.5 (and 1) hr. with 2 cc. concentrated HCl, diluted with H2O, and decanted, the residual resin triturated with H2O, dried on a clay plate, dissolved in C6H6, and chromatographed on Al2O3 gave a small amount of 3-methyl-N-(3-oxo-1-butenyl)indole, m. 176-8° (MeOH). Skatole (10 g.) and 15 cc. I treated during 75 min. with stirring with 20 cc. 6N HCl, diluted with H2O, and decanted, and the dried, resinous residue extracted with Et2O left 2.8 g. brown powder, which yielded from EtOAc yellow-brown needles. IV (850 mg.), 2 cc. I, and 1 cc. concentrated HCl kept 0.5 hr. and diluted with H2O yielded 800 mg. N-AcCH:CH derivative (XIX) of IV, yellowish prisms, m. 125°. XIX and NH2OH.HCl in C5H5N kept overnight yielded IV, m. 98-9°. XIX in MeOH was not affected by NaBH4. Indoline and III with I gave similarly the 1-AcCH:CH derivs., m. 100° (ligroine), and 180° (EtOH), resp. N-Methyl-1,2,3,4-tetrahydrocarbazole, 11-methyl-1,2,3,4-tetrahydrocarbazolenine, and 1- and 4-oxo-1,2,3,4-tetrahydrocarbazole did not react with I and concentrated HCl; in some cases some 1,3,5-C6H3Ac3, m. 161° (H2O), was obtained. V did not react with Me2CO, Ac2CH2, or AcCH2CO2Et under the same conditions as I, not even in refluxing EtOH in the presence of concentrated HCl. The ultraviolet spectra of VI, VII, VIII, IX, X, XII, XIII, XIV, XV, XVII, and XIX, and the infrared spectra in the 5.5-6.5 μ region of VI, VII, X, XII, and XIX are recorded.

RX(2) OF 3 C + D ===> E



C D



E
YIELD 85%

RX(2) RCT C 942-01-8, D 5436-21-5
PRO E 2646-01-7
SOL 7647-01-0 HCl
NTE Classification: Elimination; Geoselectiveintermediate;

N-Alkylation; # Conditions: MeCOCH2CH(OMe)2; HCl 2-3mn + 15mn

L46 ANSWER 24 OF 24 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 34:35971 CASREACT Full-text

TITLE: Preparation of α,β-dichloroethylanisoles and transformation to α- and β-chloromethoxystyrenes

AUTHOR(S): Quelet, Raymond; Allard, Jean

SOURCE: Bull. soc. chim. (1940), 7, 215-27

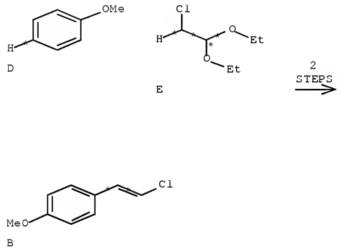
DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB A mixture of 108 g. anisole, 152 g. of ClCH2CH(OEt)2, 100 g. of concentrated HCl and 50 g. H2O was stirred for 2 hrs. at 60-70° in the presence of dry HCl. The reaction product was washed, dried and freed from unreacted anisole and ClCH2CH(OEt)2 by rapid distillation in vacuo, yielding 32% of crude α,β-dichloroethylanisole (I). A mixture of I with 100 g. pyridine was heated for 6 hrs. at 115°, treated with dilute HCl, washed and extracted with ether. The dried extract was distilled, producing 55 g. of crude p-methoxy-β-chlorostyrene (II) and 20 g. of crystalline residue (III). II gave 20 g. of solid crystals, which on recrystn. from alc. gave brilliant white platelets of pure II, C9H9ClO, m. 32°, nD35 1.5820, and 35 g. of a liquid mixture, b16 133-5°, nD20 1.5720, nD35 1.5625, consisting of II and a trace of a non-chlorinated derivative Recrystn. of III from benzene produced white platelets of 4,4'-dimethoxystilbene, m. 212°. Treatment of I with 2 mols. of NaOEt in absolute alc. for 4 hrs. at 100°, evaporation, dilution with H2O, extraction with ether and distillation gave 40 g. anisole, 60 g. of crude p-methoxy-α-chlorostyrene (IV) and 20 g. of residue (V), b16 above 170°. On cooling, the crude IV gave 45 g. of pure IV, m. 45°, decomposing on standing with evolution of HCl and formation of a resin which, on steam distillation, gave p-MeOC6H4Ac, m. 35°, a red powder and a resin, m. 70°. IV was reduced catalytically to p-ethylanisole. Recrystn. of V from benzene produced α,α-bis(4-methoxyphenyl)ethylene (VI), m. 143° oxidized by K2Cr2O7 to 4,4'-dimethoxybenzophenone, m. 144°. Treatment of I with 112 g. KOH in 100 g. H2O and 300 g. of 95% alc. for 4 hrs. at 100°, evaporation, dilution with H2O, extraction with ether and filtration gave 17 g. VI, insol. in ether. Evaporation and fractional distillation of the extract yielded 11 g. anisole; 34 g. IV; 30 g. of p-methoxy(α-ethoxy-β- chloroethyl)benzene (VII), b16 145-8°, d420 1.113, nD20 1.5230; and a residue of 25 g. of VI. Treatment of 1 mol. I with 70 g. KCN in 100 g. H2O and 250 g. of 95% alc. by heating to boiling and refluxing for 1 hr. after the exothermic reaction gave 40 g. anisole; 5 g. of a product, b15 120-30°, nD20 1.5080; 10 g. of residual 4,4'-dimethoxystilbene, m. 212°, and 53 g. of a fraction, b16 145-50°, nD20 1.5250, which was refractionated to yield 30 g. VII, pyrolyzed to give 70% of II, converted by boiling for 3 hrs. with alc. NaOEt to p-methoxy-α- ethoxystyrene, b16 135-7°, nD20 1.5395, d420 1.050, catalytically reduced in the presence of PtO2 to p-ethylanisole, b16 83-5°, nD20 1.5100, and mainly to p-methoxy-α-ethoxyethylbenzene, b16 114-15°, nD20 1.5080, d420 0.995. Extension of the method of condensation of ClCH2CH(OEt)2 to other phenolic ethers gave only 5% yields of the corresponding α,β-di-Cl compds. These are preferably made in 25% yields by chlorination of the corresponding methoxystyrenes obtained by dechlorohydration of the α-chloroethyl homologs of anisole: 3-methyl-4-methoxy-α-chlorostyrene, b18 145-50°, nD20 1.5650, d420 1.163; 3-methyl-4-methoxy-β-chlorostyrene, b18 155-8°, m. 65.5°; 5-methyl-2-methoxy-α-chlorostyrene, b16 135-7°, nD20 1.5488, d420 1.113; 5-methyl-2-methoxy-β-chlorostyrene, b16 143-5°, nD20 1.5715, d420 1.178; 2-methyl-5-isopropyl-4-

methoxy-α-chlorostyrene, b16 158-60°, nD20 1.5230 (in this reaction there is also produced an appreciable amount of 2-methyl-5-isopropyl-4-methoxy-1-(α-ethoxy-β- chloroethyl)benzene, b16 164-5°, nD20 1.5260, pyrolyzed to the corresponding β-chlorostyrene, b16 155-60°, nD20 1.5578, d420 1.095. There is also formed some amount of a compound, probably 2-methyl-5-isopropyl-4-methoxy-α-ethoxystyrene, b16 145-50°, nD20 1.5235.)

RX(4) OF 5 COMPOSED OF RX(2), RX(1)
RX(4)   D + E ===> B



RX(2)	RCT	D 100-66-3, E 621-62-5
	RGT	F 7647-01-0 HCl
	PRO	A 119015-52-0
	SOL	7732-18-5 Water
	NTE	Classification: C-Alkylation; Chlorination; Regioselective; # Conditions: H2O HCl saturated; 60-70 deg 2h; # Comments: other examples with lower yields; ZnCl2 or H3PO4 gives a poorer yield
RX(1)	RCT	A 119015-52-0
	RGT	C 110-86-1 Pyridine
	PRO	B 18684-94-1
	NTE	Classification: Elimination; Dehydrochlorination; # Conditions: pyridine

```
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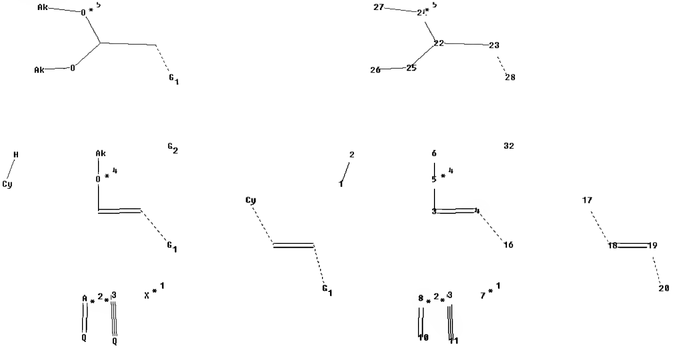

chain nodes :
1 2 3 4 5 6 7 16 17 18 19 20 22 23 24 25 26 27 28 32
ring/chain nodes :
8 9 10 11
chain bonds :
1-2 3-4 3-5 4-16 5-6 17-18 18-19 19-20 22-23 22-24 22-25 23-28 24-27
25-26
ring/chain bonds :
8-10 9-11
exact/norm bonds :
1-2 3-5 4-16 5-6 8-10 9-11 17-18 19-20 22-24 22-25 23-28 24-27 25-26

exact bonds :
3-4 18-19 22-23

G1:[*1],[*2],[*3]

G2:[*4],[*5]

Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS
11:CLASS 16:CLASS 17:Atom 18:CLASS 19:CLASS 20:CLASS 22:CLASS 23:CLASS
24:CLASS 25:CLASS
26:CLASS 27:CLASS 28:CLASS 32:CLASS
Generic attributes :
1:
Saturation : Unsaturated
17:
Saturation : Unsaturated

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containing 32

fragments assigned product role:
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reaction site bonds:
17-18:CC

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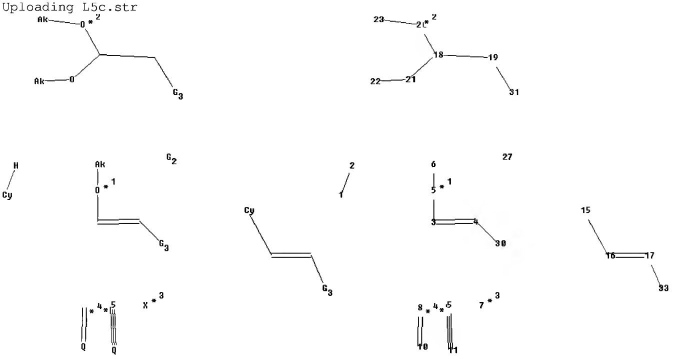

chain nodes :
1 2 3 4 5 6 7 8 9 10 11 15 16 17 18 19 20 21 22 23 27 30 31
33
chain bonds :
1-2 3-4 3-5 4-30 5-6 8-10 9-11 15-16 16-17 17-33 18-19 18-20 18-21 19-
31
20-23 21-22
exact/norm bonds :
1-2 3-5 4-30 5-6 8-10 9-11 15-16 17-33 18-20 18-21 19-31 20-23 21-22

exact bonds :
3-4 16-17 18-19

G2:[*1],[*2]

G3:[*3],[*4],[*5]

Hydrogen count :
3:= exact 1 4:= exact 1 16:= exact 1 17:= exact 1 18:= exact 1 19:= exact 2

Connectivity :
3:2 E exact RC ring/chain 4:2 E exact RC ring/chain 16:2 E exact RC ring/chain
17:2 E exact RC ring/chain 18:3 E exact RC ring/chain 19:2 E exact RC ring/chain
Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS

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11:CLASS  15:Atom  16:CLASS  17:CLASS  18:CLASS  19:CLASS  20:CLASS  21:CLASS
22:CLASS  23:CLASS
27:CLASS  30:CLASS  31:CLASS  33:CLASS
Generic attributes :
1:
Saturation             : Unsaturated
15:
Saturation             : Unsaturated

fragments assigned reactant role:
containing 1
containing 27
fragments assigned product role:
containing 15
reaction site bonds:
15-16:CC



=> d stat que L22
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L2  (    190274)SEA FILE=CASREACT ABB=ON  PLU=ON  ACYCLIC ALKENE/FG.PRO
L3              SCR 278 OR 1342
L4           143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 (   742 REACTIONS)
L5              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L7            43 SEA FILE=CASREACT SUB=L4 SSS FUL L5 (   207 REACTIONS)
L8              TRANSFER  PLU=ON  L4 1- RX :    1312 TERMS
L9          1312 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8/RN
L10          441 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND X/ELS
L11          421 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND C/ELS
L12           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 NOT L11
L13       188275 SEA FILE=CASREACT ABB=ON  PLU=ON  L12
L14           24 SEA FILE=CASREACT ABB=ON  PLU=ON  L13 (L) L7
L16           11 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND M/ELS
L17            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 NOT L16
L18       153759 SEA FILE=CASREACT ABB=ON  PLU=ON  L17
L19           31 SEA FILE=CASREACT ABB=ON  PLU=ON  L18 (L) L4
L22           16 SEA FILE=CASREACT ABB=ON  PLU=ON  L19 NOT L14


=> d stat que L43
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
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L3              SCR 278 OR 1342
L4           143 SEA FILE=CASREACT SUB=L2 SSS FUL L1 AND L3 (   742 REACTIONS)
L8              TRANSFER  PLU=ON  L4 1- RX :    1312 TERMS
L9          1312 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8/RN
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```
L10          441 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 AND X/ELS
L11          421 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND C/ELS
L12           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 NOT L11
L16           11 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND M/ELS
L17            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 NOT L16
L18       153759 SEA FILE=CASREACT ABB=ON  PLU=ON  L17
L19           31 SEA FILE=CASREACT ABB=ON  PLU=ON  L18 (L) L4
L37        75833 SEA FILE=CASREACT ABB=ON  PLU=ON  64-19-7
L43            7 SEA FILE=CASREACT ABB=ON  PLU=ON  L37 (L) L19


=> s L22 or L43
L47          18 L22 OR L43

=> s L47 not L46
L48          16 L47 NOT L46

=> d ibib abs hit L48 1-16


L48  ANSWER 1 OF 16  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         146:441705  CASREACT  Full-text
TITLE:                    Regiospecific preparation of 1,4,5-trisubstituted
                          pyrazoles from 2-(1H-1,2,3-benzotriazol-1-yl)-3-(4-
                          aryl)-2-propenal derivatives
AUTHOR(S):                Katritzky, Alan R.; Vakulenko, Anatoliy V.; Akue-Gedu,
                          Rufine; Gromova, Anna V.; Witek, Rachel; Rogers, James
                          W.
CORPORATE SOURCE:         Center for Heterocyclic Compounds, Department of
                          Chemistry, University of Florida, Gainesville, FL,
                          32611-7200, USA
SOURCE:                   ARKIVOC (Gainesville, FL, United States) (2007), (1),
                          9-21
                          CODEN: AGFUAR
                          URL: http://content.arkat-
                          usa.org/ARKIVOC/JOURNAL_CONTENT/manuscripts/2007/07-
                          2282DP%20as%20published%20mainmanuscript.pdf
PUBLISHER:                Arkat USA Inc.
DOCUMENT TYPE:            Journal; (online computer file)
LANGUAGE:                 English
AB    Treatment of α-(benzotriazolyl)-α,β-unsatd. aldehydes with monosubstituted
      hydrazine derivs., followed by alkylation at the 4-position of the pyrazoline
      ring and elimination of the benzotriazole group affords 1,4,5-trisubstituted
      pyrazoles in overall yields of 52-79%.
REFERENCE COUNT:          37     THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


RX(68) OF 112 COMPOSED OF RX(1), RX(2), RX(8)
RX(68)    2 A  +  B  +  C  +  H  ===>  Y
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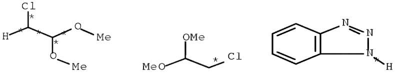
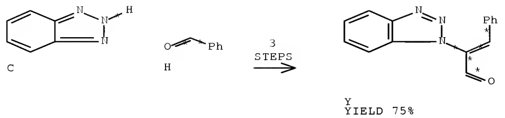


A A B



RX(1)   RCT A 97-97-2, B 95-14-7, C 273-02-9
           RGT F 298-14-6 KHCO3
           PRO D 304690-46-8, E 304690-47-9
           SOL 68-12-2 DMF
           CON SUBSTAGE(1) 18 hours, reflux
                SUBSTAGE(2) cooled

RX(2)   RCT D 304690-46-8

  STAGE(1)
     RGT J 109-72-8 BuLi
     SOL 109-99-9 THF, 110-54-3 Hexane
     CON SUBSTAGE(1) -78 deg C
          SUBSTAGE(2) 1 hour, -78 deg C

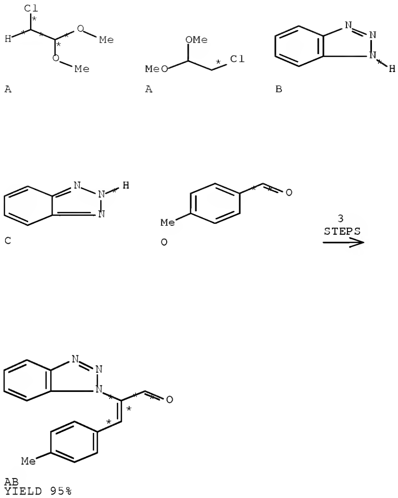
  STAGE(2)
     RCT H 100-52-7
     SOL 109-99-9 THF
     CON SUBSTAGE(1) -78 deg C
          SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

  STAGE(3)
     RGT K 12125-02-9 NH4Cl
     SOL 7732-18-5 Water
     CON room temperature

           PRO I 934565-49-8
           NTE stereoselective, 70:30 E:Z

RX(8)   RCT I 934565-49-8
           RGT Z 7647-01-0 HCl
           PRO Y 163373-60-0
           SOL 7732-18-5 Water, 109-99-9 THF
           CON SUBSTAGE(1) room temperature
                SUBSTAGE(2) 48 hours, room temperature
           NTE stereoselective

RX(69) OF 112 COMPOSED OF RX(1), RX(3), RX(10)
RX(69)   2 A + B + C + O ===> AB




```
RX(1)     RCT  A 97-97-2, B 95-14-7, C 273-02-9
          RGT  F 298-14-6 KHCO3
          PRO  D 304690-46-8, E 304690-47-9
          SOL  68-12-2 DMF
          CON  SUBSTAGE(1) 18 hours, reflux
               SUBSTAGE(2) cooled

RX(3)     RCT  D 304690-46-8

            STAGE(1)
               RGT  J 109-72-8 BuLi
               SOL  109-99-9 THF, 110-54-3 Hexane
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 1 hour, -78 deg C

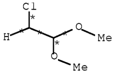
            STAGE(2)
               RCT  O 104-87-0
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 2 hours, -78 deg C -> room temperature
```

```
            STAGE(3)
               RGT  K 12125-02-9 NH4Cl
               SOL  7732-18-5 Water
               CON  room temperature

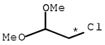
          PRO  P 934565-50-1
          NTE  stereoselective, 70:30 E:Z

RX(10)    RCT  P 934565-50-1
          RGT  Z 7647-01-0 HCl
          PRO  AB 934565-56-7
          SOL  7732-18-5 Water, 109-99-9 THF
          CON  SUBSTAGE(1) room temperature
               SUBSTAGE(2) 48 hours, room temperature
          NTE  stereoselective


RX(71) OF 112 COMPOSED OF RX(1), RX(5), RX(12)
RX(71)    2 A  +  B  +  C  +  S  ===>  AD
```



A



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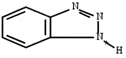

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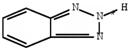

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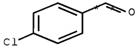
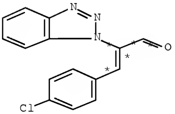


S

3
STEPS
→



AD
YIELD 85%

```
RX(1)      RCT  A 97-97-2, B 95-14-7, C 273-02-9
           RGT  F 298-14-6 KHCO3
           PRO  D 304690-46-8, E 304690-47-9
           SOL  68-12-2 DMF
           CON  SUBSTAGE(1) 18 hours, reflux
                SUBSTAGE(2) cooled

RX(5)      RCT  D 304690-46-8

             STAGE(1)
                RGT  J 109-72-8 BuLi
                SOL  109-99-9 THF, 110-54-3 Hexane
                CON  SUBSTAGE(1) -78 deg C
                     SUBSTAGE(2) 1 hour, -78 deg C

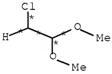
             STAGE(2)
                RCT  S 104-88-1
                SOL  109-99-9 THF
                CON  SUBSTAGE(1) -78 deg C
                     SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

             STAGE(3)
                RGT  K 12125-02-9 NH4Cl
                SOL  7732-18-5 Water
                CON  room temperature

           PRO  T 934565-52-3
           NTE  stereoselective, 70:30 E:Z

RX(12)     RCT  T 934565-52-3
           RGT  Z 7647-01-0 HCl
           PRO  AD 161373-55-3
           SOL  7732-18-5 Water, 109-99-9 THF
           CON  SUBSTAGE(1) room temperature
                SUBSTAGE(2) 48 hours, room temperature
           NTE  stereoselective


RX(72) OF 112 COMPOSED OF RX(1), RX(6), RX(13)
RX(72)     2 A  +  B  +  C  +  U  ===>  AE
```



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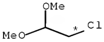

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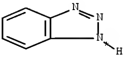

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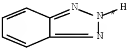

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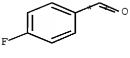
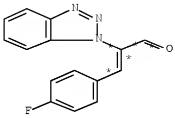


U

3
STEPS



AE
YIELD 90%

```
RX(1)     RCT  A 97-97-2, B 95-14-7, C 273-02-9
          RGT  F 298-14-6 KHCO3
          PRO  D 304690-46-8, E 304690-47-9
          SOL  68-12-2 DMF
          CON  SUBSTAGE(1) 18 hours, reflux
               SUBSTAGE(2) cooled

RX(6)     RCT  D 304690-46-8

            STAGE(1)
               RGT  J 109-72-8 BuLi
               SOL  109-99-9 THF, 110-54-3 Hexane
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 1 hour, -78 deg C

            STAGE(2)
               RCT  U 459-57-4
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

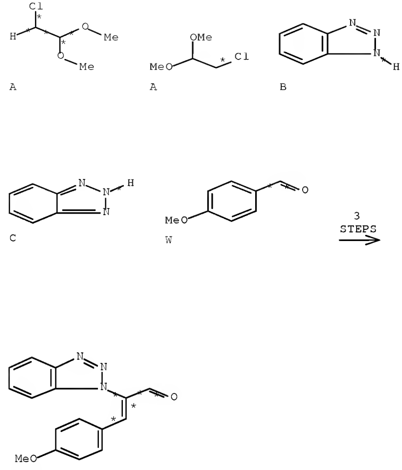
            STAGE(3)
               RGT  K 12125-02-9 NH4Cl
               SOL  7732-18-5 Water
               CON  room temperature

          PRO  V 934565-53-4
          NTE  stereoselective, 70:30 E:Z

RX(13)    RCT  V 934565-53-4
          RGT  Z 7647-01-0 HCl
          PRO  AE 161373-56-4
          SOL  7732-18-5 Water, 109-99-9 THF
          CON  SUBSTAGE(1) room temperature
               SUBSTAGE(2) 48 hours, room temperature
          NTE  stereoselective
```

RX(73) OF 112 COMPOSED OF RX(1), RX(7), RX(14)

RX(73)   2 A + B + C + W ===> AF



AF
YIELD 94%

```
RX(1)     RCT  A 97-97-2, B 95-14-7, C 273-02-9
          RGT  F 298-14-6 KHCO3
          PRO  D 304690-46-8, E 304690-47-9
          SOL  68-12-2 DMF
          CON  SUBSTAGE(1) 18 hours, reflux
               SUBSTAGE(2) cooled

RX(7)     RCT  D 304690-46-8

            STAGE(1)
               RGT  J 109-72-8 BuLi
               SOL  109-99-9 THF, 110-54-3 Hexane
               CON  SUBSTAGE(1) -78 deg C
                    SUBSTAGE(2) 1 hour, -78 deg C

            STAGE(2)
               RCT  W 123-11-5
               SOL  109-99-9 THF
```

```
            CON  SUBSTAGE(1) -78 deg C
                 SUBSTAGE(2) 2 hours, -78 deg C -> room temperature

          STAGE(3)
            RGT  K 12125-02-9 NH4Cl
            SOL  7732-18-5 Water
            CON  room temperature

        PRO  X 934565-54-5
        NTE  stereoselective, 70:30 E:Z

RX(14)  RCT  X 934565-54-5
        RGT  Z 7647-01-0 HCl
        PRO  AF 934565-58-9
        SOL  7732-18-5 Water, 109-99-9 THF
        CON  SUBSTAGE(1) room temperature
             SUBSTAGE(2) 48 hours, room temperature
        NTE  stereoselective
```

L48 ANSWER 2 OF 16 CASREACT

ACCESSION NUMBER: 145:489028 CASREACT Full-text

TITLE: Synthesis of rigid trichostatin A analogs as HDAC inhibitors

AUTHOR(S): Charrier, Cedric; Bertrand, Philippe; Gesson, Jean-Pierre; Roche, Joelle

CORPORATE SOURCE: Laboratoire Synthese et Reactivite des Substances Naturelles, UMR 6514, Universite de Poitiers et CNRS, Poitiers, 86022, Fr.

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(20), 5339-5344
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Ltd.

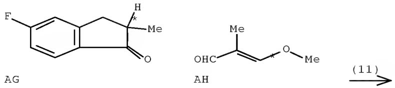
DOCUMENT TYPE: Journal

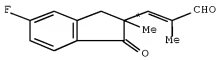
LANGUAGE: English

AB New inhibitors of histone deacetylase (HDAC) have been synthesized and evaluated for their activity toward non small lung cancer cell line H661. Their design is based on indanone (or tetralone) systems leading to trichostatin A (TSA) analogs with limited conformational mobility. Mol. modelization at the AM1 level revealed that the conformations of indane-based analogs and TSA bound to HDAC like protein are similar. The synthesis of these new analogs was achieved by alkylation of an appropriate indanone (or tetralone) to introduce the side chain bearing a terminal ester group, the latter being a precursor of hydroxamic acid and aminobenzamide derivs. Hydroxamic acids with the TSA side chain were found to be the most active compds. and the presence of the dimethylamino group on the Ph ring turned out to be essential to achieve low micromolar activities against H661 cancer cells.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(11) OF 153 ...AG + AH ===> AI...





YIELD 82%

RX(11) RCT AG 41201-58-5

STAGE(1)
RGT Q 4111-54-0 LiN(Pr-i)2
SOL 109-99-9 THF
CON 1.5 hours, -80 deg C

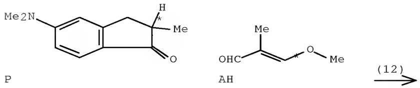
STAGE(2)
RCT AH 914261-53-3
SOL 109-99-9 THF
CON SUBSTAGE(1) 3 hours, -80 deg C
SUBSTAGE(2) overnight, -80 deg C -> room temperature

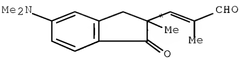
STAGE(3)
RGT V 12125-02-9 NH4Cl
SOL 7732-18-5 Water

STAGE(4)
CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)
SOL 108-88-3 PhMe
CON 1 hour, reflux

PRO AI 914261-70-4

RX(12) OF 153 ...P + AH ===> AK...





AK
YIELD 80%

RX(12) RCT P 914261-49-7

  STAGE(1)
    RGT Q 4111-54-0 LiN(Pr-i)2
    SOL 109-99-9 THF
    CON 1.5 hours, -80 deg C

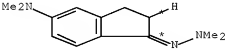
  STAGE(2)
    RCT AH 914261-53-3
    SOL 109-99-9 THF
    CON SUBSTAGE(1) 3 hours, -80 deg C
         SUBSTAGE(2) overnight, -80 deg C -> room temperature

  STAGE(3)
    RGT V 12125-02-9 NH4Cl
    SOL 7732-18-5 Water

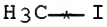
  STAGE(4)
    CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium
         salt (1:3)
    SOL 108-88-3 PhMe
    CON 1 hour, reflux

  PRO AK 914261-54-4

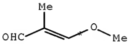
RX(41) OF 153 COMPOSED OF RX(4), RX(12)
RX(41) L + O + AH ===> AK



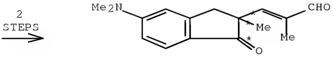
L



O



AH



AK
YIELD 80%

```
RX(4)     RCT  L 914261-36-2, O 74-88-4

            STAGE(1)
               RGT  Q 4111-54-0 LiN(Pr-i)2
               CON  -40 deg C

            STAGE(2)
               RGT  R 12408-02-5 H+

          PRO  P 914261-49-7

RX(12)    RCT  P 914261-49-7

            STAGE(1)
               RGT  Q 4111-54-0 LiN(Pr-i)2
               SOL  109-99-9 THF
               CON  1.5 hours, -80 deg C

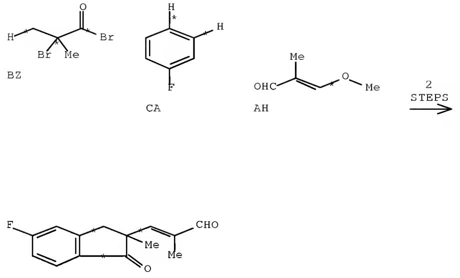
            STAGE(2)
               RCT  AH 914261-53-3
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) 3 hours, -80 deg C
                    SUBSTAGE(2) overnight, -80 deg C -> room temperature

            STAGE(3)
               RGT  V 12125-02-9 NH4Cl
               SOL  7732-18-5 Water

            STAGE(4)
               CAT  196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium
                    salt (1:3)
               SOL  108-88-3 PhMe
               CON  1 hour, reflux

          PRO  AK 914261-54-4


RX(69) OF 153 COMPOSED OF RX(37), RX(11)
RX(69)    BZ  +  CA  +  AH  ===>  AI
```




```
RX(37)    RCT  BZ 20769-85-1, CA 462-06-6
          RGT  CB 7446-70-0 AlCl3
          PRO  AG 41201-58-5
          SOL  75-15-0 CS2

RX(11)    RCT  AG 41201-58-5

            STAGE(1)
               RGT  Q 4111-54-0 LiN(Pr-i)2
               SOL  109-99-9 THF
               CON  1.5 hours, -80 deg C

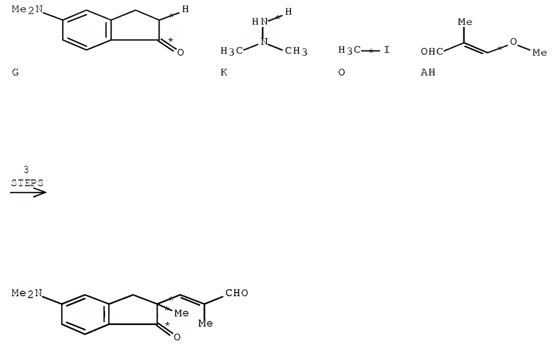
            STAGE(2)
               RCT  AH 914261-53-3
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) 3 hours, -80 deg C
                    SUBSTAGE(2) overnight, -80 deg C -> room temperature

            STAGE(3)
               RGT  V 12125-02-9 NH4Cl
               SOL  7732-18-5 Water

            STAGE(4)
               CAT  196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium
                    salt (1:3)
               SOL  108-88-3 PhMe
               CON  1 hour, reflux

          PRO  AI 914261-70-4


RX(73) OF 153 COMPOSED OF RX(3), RX(4), RX(12)
RX(73)    G  +  K  +  O  +  AH  ===>  AK
```



AK
YIELD 80%

```
RX(3)      RCT  G 51981-67-0, K 57-14-7
           PRO  L 914261-36-2
           CAT  104-15-4 TsOH
           SOL  108-88-3 PhMe
           NTE  Dean-Stark trap used

RX(4)      RCT  L 914261-36-2, O 74-88-4

             STAGE(1)
                RGT  Q 4111-54-0 LiN(Pr-i)2
                CON  -40 deg C

             STAGE(2)
                RGT  R 12408-02-5 H+

           PRO  P 914261-49-7

RX(12)     RCT  P 914261-49-7

             STAGE(1)
                RGT  Q 4111-54-0 LiN(Pr-i)2
                SOL  109-99-9 THF
                CON  1.5 hours, -80 deg C

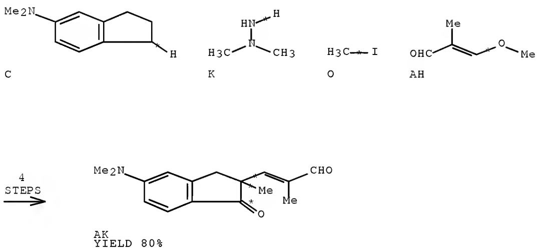
             STAGE(2)
                RCT  AH 914261-53-3
                SOL  109-99-9 THF
                CON  SUBSTAGE(1) 3 hours, -80 deg C
                     SUBSTAGE(2) overnight, -80 deg C -> room temperature
```

STAGE(3)
RGT V 12125-02-9 NH4Cl
SOL 7732-18-5 Water

STAGE(4)
CAT 196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium salt (1:3)
SOL 108-88-3 PhMe
CON 1 hour, reflux

PRO AK 914261-54-4

RX(74) OF 153 COMPOSED OF RX(2), RX(3), RX(4), RX(12)
RX(74) C + K + O + AH ===> AK



RX(2) RCT C 871886-03-2
RGT H 84-58-2 DDQ
PRO G 51981-67-0
SOL 7732-18-5 Water, 109-99-9 THF
CON 1 hour, room temperature

RX(3) RCT G 51981-67-0, K 57-14-7
PRO L 914261-36-2
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe
NTE Dean-Stark trap used

RX(4) RCT L 914261-36-2, O 74-88-4

STAGE(1)
RGT Q 4111-54-0 LiN(Pr-i)2
CON -40 deg C

STAGE(2)
RGT R 12408-02-5 H+

```
         PRO   P 914261-49-7

RX(12)   RCT   P 914261-49-7

           STAGE(1)
              RGT   Q 4111-54-0 LiN(Pr-i)2
              SOL   109-99-9 THF
              CON   1.5 hours, -80 deg C

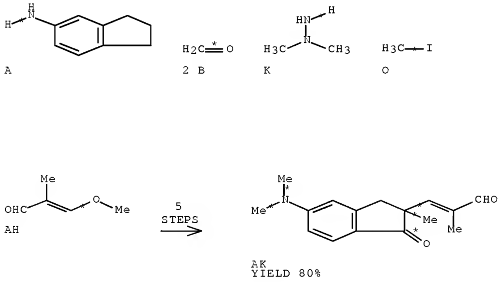
           STAGE(2)
              RCT   AH 914261-53-3
              SOL   109-99-9 THF
              CON   SUBSTAGE(1) 3 hours, -80 deg C
                    SUBSTAGE(2) overnight, -80 deg C -> room temperature

           STAGE(3)
              RGT   V 12125-02-9 NH4Cl
              SOL   7732-18-5 Water

           STAGE(4)
              CAT   196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium
                    salt (1:3)
              SOL   108-88-3 PhMe
              CON   1 hour, reflux

         PRO   AK 914261-54-4


RX(119) OF 153 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(12)
RX(119)    A  +  2 B  +  K  +  O  +  AH  ===>  AK
```




```
RX(1)    RCT   A 24425-40-9, B 50-00-0

           STAGE(1)
              RGT   D 25895-60-7 NaBH3CN
              SOL   75-05-8 MeCN
```

```
            CON  15 minutes, room temperature

          STAGE(2)
            RGT  E 64-19-7 AcOH
            CON  neutralized

         PRO  C 871886-03-2

RX(2)    RCT  C 871886-03-2
         RGT  H 84-58-2 DDQ
         PRO  G 51981-67-0
         SOL  7732-18-5 Water, 109-99-9 THF
         CON  1 hour, room temperature

RX(3)    RCT  G 51981-67-0, K 57-14-7
         PRO  L 914261-36-2
         CAT  104-15-4 TsOH
         SOL  108-88-3 PhMe
         NTE  Dean-Stark trap used

RX(4)    RCT  L 914261-36-2, O 74-88-4

          STAGE(1)
            RGT  Q 4111-54-0 LiN(Pr-i)2
            CON  -40 deg C

          STAGE(2)
            RGT  R 12408-02-5 H+

         PRO  P 914261-49-7

RX(12)   RCT  P 914261-49-7

          STAGE(1)
            RGT  Q 4111-54-0 LiN(Pr-i)2
            SOL  109-99-9 THF
            CON  1.5 hours, -80 deg C

          STAGE(2)
            RCT  AH 914261-53-3
            SOL  109-99-9 THF
            CON  SUBSTAGE(1) 3 hours, -80 deg C
                 SUBSTAGE(2) overnight, -80 deg C -> room temperature

          STAGE(3)
            RGT  V 12125-02-9 NH4Cl
            SOL  7732-18-5 Water

          STAGE(4)
            CAT  196504-57-1 1,3,6-Pyrenetrisulfonic acid, 8-amino-, sodium
                 salt (1:3)
            SOL  108-88-3 PhMe
            CON  1 hour, reflux

         PRO  AK 914261-54-4
```

L48 ANSWER 3 OF 16 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 143:477858 CASREACT Full-text
TITLE: Preparation of substituted pyrido[3,2-b]indoles for

use in pharmaceutical compositions for the treatment of HIV-infection

INVENTOR(S): Kesteleyn, Bart Rudolf Romanie; Van De Vreken, Wim; Kindermans, Natalie Maria Francisca; Canard, Maxime Francis Jean-Marie Ghislain; Hertogs, Kurt; Bettens, Eva; De Vroey, Veronique Corine Paul; Jochmans, Dirk Edward Desire; Wigerinck, Piet Tom Bert Paul; Wang, Jing; Tahri, Abdellah; Surleraux, Dominique Louis Nestor Ghislain

PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.

SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

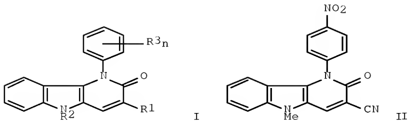
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110411	A1	20051124	WO 2005-EP52266	20050517
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005244449	A1	20051124	AU 2005-244449	20050517
CA 2563601	A1	20051124	CA 2005-2563601	20050517
EP 1750708	A1	20070214	EP 2005-747916	20050517
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1953751	A	20070425	CN 2005-80015688	20050517
BR 2005011144	A	20071127	BR 2005-11144	20050517
JP 2007538053	T	20071227	JP 2007-517256	20050517
IN 2006DN06106	A	20070831	IN 2006-DN6106	20061019
US 20070249655	A1	20071025	US 2006-569111	20061114
MX 2006PA13316	A	20070202	MX 2006-PA13316	20061116
KR 2007011588	A	20070124	KR 2006-725921	20061208

PRIORITY APPLN. INFO.: EP 2004-102173 20040517
US 2004-102173 20040517
WO 2005-EP52266 20050517

OTHER SOURCE(S): MARPAT 143:477858

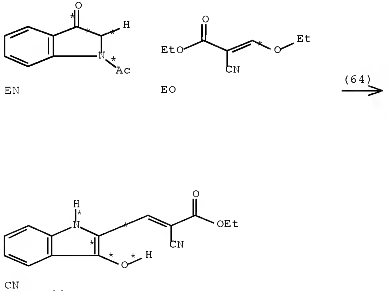
GI



AB Pyrido[3,2-b]indoles, such as I [R1 = H, CN, halogen, alkylcarbonyl, etc.; R2 = H, (hetero)alkyl, alkenyl, etc.; R3 = NO2, CN, OH, (un)substituted amino, etc.; n = 1-3; and their N-oxides, salts, stereoisomers, racemic mixts., prodrugs, esters or metabolites thereof], were prepared for therapeutic use and anti-HIV agents. Thus, pyrido[3,2-b]indole II was prepared via a five step synthetic scheme starting from the reaction of 1-acetyl-3-hydroxyindole with 4-nitroaniline. The prepared pyrido[3,2-b]indoles were tested for inhibition of HIV reverse transcriptase, for metabolism using human liver microsomal fractions and for anti-HIV activity. Thus, I and their pharmaceutical compns. are useful for the treatment of retroviral infections such as HIV infection, in particular, in the treatment of infections with multi-drug resistant retroviruses.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(64) OF 302 EN + EO ===> CN...



CN
YIELD 92%

RX(64) RCT EN 16800-68-3

```
      STAGE(1)
         RGT  DW 7646-69-7 NaH
         SOL  109-99-9 THF
         CON  30 minutes, -78 deg C

      STAGE(2)
         RCT  EO 94-05-3
         CON  SUBSTAGE(1) 15 minutes, -78 deg C
              SUBSTAGE(2) 1 hour, -78 deg C
              SUBSTAGE(3) overnight, -78 deg C -> room temperature

      STAGE(3)
         RGT  L 7647-01-0 HCl
         SOL  7732-18-5 Water
         CON  cooled, pH 1

    PRO  CN 136429-63-5


L48  ANSWER 4 OF 16  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         142:298286  CASREACT  Full-text
TITLE:                    Preparation of tricyclic nucleosides or nucleotides as
                          antiviral and antitumor therapeutic agents
INVENTOR(S):              Cook, Phillip Dan; Ewing, Gregory; Jin, Yi; Lambert,
                          John; Prhavc, Marija; Rajappan, Vasanthakumar;
                          Rajwanshi, Vivek K.; Sakthivel, Kandasamy
PATENT ASSIGNEE(S):       Biota, Inc., USA
SOURCE:                   PCT Int. Appl., 106 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
     WO 2005021568     A2   20050310      WO 2004-US27819  20040827
     WO 2005021568     A3   20050421
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     AU 2004269026     A1   20050310      AU 2004-269026   20040827
     CA 2537114        A1   20050310      CA 2004-2537114  20040827
     EP 1660511        A2   20060531      EP 2004-782317   20040827
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
     BR 2004014019     A    20061024      BR 2004-14019    20040827
     CN 1863813        A    20061115      CN 2004-80029262 20040827
     JP 2007504152     T    20070301      JP 2006-524865   20040827
     MX 2006PA02198    A    20070814      MX 2006-PA2198   20060224
     NO 2006000979     A    20060502      NO 2006-979      20060228
     IN 2006KN00570    A    20070706      IN 2006-KN570    20060309
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     US 20080200423    A1   20080821       US 2006-568917    20061129
     US 20070135363    A1   20070614       US 2007-674954    20070214
     US 7268119        B2   20070911
PRIORITY APPLN. INFO.:                     US 2003-498425P   20030827
                                           WO 2004-US27819   20040827
                                           US 2006-568917    20061129
OTHER SOURCE(S):          MARPAT 142:298286
GI
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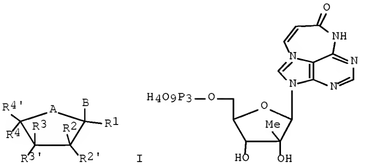
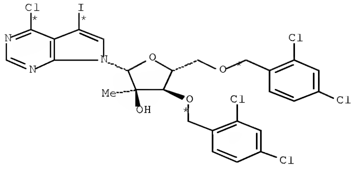


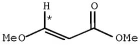
I II

AB Nucleosides and nucleotides containing a tricyclic base portion I, wherein A is O, S, CH2, NH, CHF, CF2; R1, R2, R2', R3, R3', R4 are independently H, F, Cl, iodo, Br, OH, SH, NH2, NHOH, NHNH2, N3, COOH, CN, CONH2, CSNH2, COOR, R, OR, SR, SSR, NHR, NR2; R4' is L-R5; L is O, S, NH, NR, CY2S, CY2NH, CY2, CY2CY2, CY2OCY2, CY2SCY2, CY2NHCY2; Y is H, F, Cl, Br, alkyl, alkenyl, alkynyl, R4' is OH, monophosphate, diphosphate, triphosphate; B is substituted tricyclic nucleobase derivs.; R is alkyl, alkenyl, alkynyl, aryl, acyl, aralkyl; thereof are useful for treating infectious diseases and proliferative disorders, such as viral infections or cancer resp. Thus, nucleotide II was prepared and tested in vitro as polymerase inhibitor, antiviral, and antitumor therapeutic agent. Title compds. were typically cytotoxic in the range of 30 to > 100 μM. II showed inhibitory of NS5B in the range of 100 to >1000 nM. Selected examples displayed IC50 values in the range of to 100 nM.

RX(305) OF 542 COMPOSED OF RX(56), RX(57), RX(62)
RX(305) CD + ER ===> ES

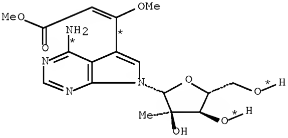


CD



ER

3
STEPS
→



ES
YIELD 45%

RX(56) RCT CD 847551-25-1

STAGE(1)
RGT AV 10294-34-5 BCl3
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 2.5 hours, -78 deg C
SUBSTAGE(2) 3 hours, -30 - -20 deg C

STAGE(2)
RGT N 67-56-1 MeOH
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(2) 0.5 hours, -15 deg C

STAGE(3)
RGT M 7664-41-7 NH3
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C, neutralized

```
                    SUBSTAGE(2) 0.25 hours, room temperature

          PRO   EJ 847551-48-8

RX(57)    RCT   EJ 847551-48-8
          RGT   M 7664-41-7 NH3
          PRO   EK 847551-49-9
          SOL   7664-41-7 NH3
          CON   SUBSTAGE(1) overnight, 85 deg C
                SUBSTAGE(2) cooled
          NTE   thermal, chemoselective, autoclave used

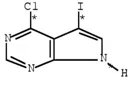
RX(62)    RCT   EK 847551-49-9, ER 5788-17-0

            STAGE(1)
               RGT  Q 121-44-8 Et3N
               CAT  14221-01-3 Pd(PPh3)4, 7681-65-4 CuI
               SOL  68-12-2 DMF
               CON  SUBSTAGE(1) room temperature
                    SUBSTAGE(2) 24 hours, 70 deg C
                    SUBSTAGE(3) 70 deg C -> room temperature

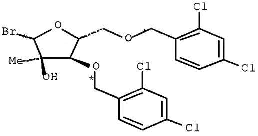
            STAGE(2)
               RGT  R 11114-15-1 DOWEX 50W
               SOL  67-56-1 MeOH, 75-09-2 CH2Cl2
               CON  45 minutes, room temperature

          PRO   ES 847551-54-6
          NTE   Dowex 1x2-100 Bicarb form of reagent used in stage 2

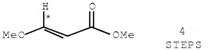

RX(309) OF 542 COMPOSED OF RX(30), RX(56), RX(57), RX(62)
RX(309)   CC  +  AG  +  ER  ===>  ES
```



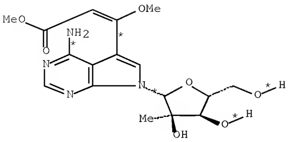
CC



AG



ER



ES
YIELD 45%

RX(30) RCT CC 123148-78-7

STAGE(1)
RGT BO 7646-69-7 NaH
SOL 75-05-8 MeCN
CON 4 hours, room temperature

STAGE(2)
RCT AG 847551-03-5
SOL 75-05-8 MeCN
CON 24 hours, room temperature

STAGE(3)
RGT J 7732-18-5 Water
CON room temperature

PRO CD 847551-25-1
NTE stereoselective

RX(56) RCT CD 847551-25-1

STAGE(1)
RGT AV 10294-34-5 BCl3
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 2.5 hours, -78 deg C
SUBSTAGE(2) 3 hours, -30 - -20 deg C

STAGE(2)
RGT N 67-56-1 MeOH
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(2) 0.5 hours, -15 deg C

STAGE(3)
RGT M 7664-41-7 NH3
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C, neutralized
SUBSTAGE(2) 0.25 hours, room temperature

PRO EJ 847551-48-8

RX(57) RCT EJ 847551-48-8
RGT M 7664-41-7 NH3

```
          PRO   EK 847551-49-9
          SOL   7664-41-7 NH3
          CON   SUBSTAGE(1) overnight, 85 deg C
                SUBSTAGE(2) cooled
          NTE   thermal, chemoselective, autoclave used

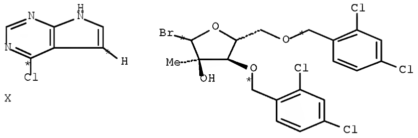
RX(62)    RCT   EK 847551-49-9, ER 5788-17-0

            STAGE(1)
               RGT  Q 121-44-8 Et3N
               CAT  14221-01-3 Pd(PPh3)4, 7681-65-4 CuI
               SOL  68-12-2 DMF
               CON  SUBSTAGE(1) room temperature
                    SUBSTAGE(2) 24 hours, 70 deg C
                    SUBSTAGE(3) 70 deg C -> room temperature

            STAGE(2)
               RGT  R 11114-15-1 DOWEX 50W
               SOL  67-56-1 MeOH, 75-09-2 CH2Cl2
               CON  45 minutes, room temperature

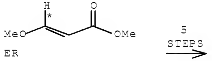
          PRO   ES 847551-54-6
          NTE   Dowex 1x2-100 Bicarb form of reagent used in stage 2


RX(409) OF 542 COMPOSED OF RX(29), RX(30), RX(56), RX(57), RX(62)
RX(409)   X  +  AG  +  ER  ===>  ES
```



X

AG



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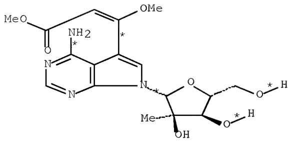

ES
YIELD 45%

```
RX(29)     RCT   X 3680-69-1
           RGT   C 516-12-1 Iodosuccinimide
           PRO   CC 123148-78-7
           SOL   109-99-9 THF
           CON   4 hours, room temperature
           NTE   regioselective

RX(30)     RCT   CC 123148-78-7

             STAGE(1)
                RGT   BO 7646-69-7 NaH
                SOL   75-05-8 MeCN
                CON   4 hours, room temperature

             STAGE(2)
                RCT   AG 847551-03-5
                SOL   75-05-8 MeCN
                CON   24 hours, room temperature

             STAGE(3)
                RGT   J 7732-18-5 Water
                CON   room temperature

           PRO   CD 847551-25-1
           NTE   stereoselective

RX(56)     RCT   CD 847551-25-1

             STAGE(1)
                RGT   AV 10294-34-5 BCl3
                SOL   75-09-2 CH2Cl2
                CON   SUBSTAGE(1) 2.5 hours, -78 deg C
                      SUBSTAGE(2) 3 hours, -30 - -20 deg C

             STAGE(2)
                RGT   N 67-56-1 MeOH
                SOL   75-09-2 CH2Cl2
                CON   SUBSTAGE(2) 0.5 hours, -15 deg C

             STAGE(3)
                RGT   M 7664-41-7 NH3
                SOL   7732-18-5 Water
                CON   SUBSTAGE(1) 0 deg C, neutralized
```

```
                    SUBSTAGE(2) 0.25 hours, room temperature

          PRO   EJ 847551-48-8

RX(57)    RCT   EJ 847551-48-8
          RGT   M 7664-41-7 NH3
          PRO   EK 847551-49-9
          SOL   7664-41-7 NH3
          CON   SUBSTAGE(1) overnight, 85 deg C
                SUBSTAGE(2) cooled
          NTE   thermal, chemoselective, autoclave used

RX(62)    RCT   EK 847551-49-9, ER 5788-17-0

            STAGE(1)
               RGT  Q 121-44-8 Et3N
               CAT  14221-01-3 Pd(PPh3)4, 7681-65-4 CuI
               SOL  68-12-2 DMF
               CON  SUBSTAGE(1) room temperature
                    SUBSTAGE(2) 24 hours, 70 deg C
                    SUBSTAGE(3) 70 deg C -> room temperature

            STAGE(2)
               RGT  R 11114-15-1 DOWEX 50W
               SOL  67-56-1 MeOH, 75-09-2 CH2Cl2
               CON  45 minutes, room temperature

          PRO   ES 847551-54-6
          NTE   Dowex 1x2-100 Bicarb form of reagent used in stage 2
```

```
L48  ANSWER 5 OF 16  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        142:56252  CASREACT  Full-text
TITLE:                   Routes to N-vinyl-nitroimidazoles and
                         N-vinyl-deazapurines
AUTHOR(S):               Clayton, Russell; Ramsden, Christopher A.
CORPORATE SOURCE:        Lennard-Jones Laboratories, School of Chemistry and
                         Physics, Keele University, Keele, ST5 5BG, UK
SOURCE:                  Journal of Heterocyclic Chemistry (2004), 41(5),
                         701-705
                         CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER:               HeteroCorporation
DOCUMENT TYPE:           Journal
LANGUAGE:                English
GI
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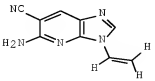
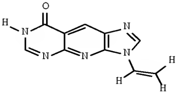


I

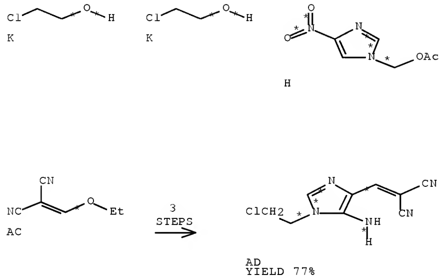


II

AB The prepns. of 4- and 5-nitro-1-vinylimidazole are described. Selective reduction of the nitro group using Fe/dil.HCl was achieved for the 4-nitro derivative but this was not effective when ethoxymethylenemalononitrile was used to trap the amine. For 5-nitroimidazole studies the N-vinyl substituent was kept masked as a 2-chloroethyl group, which remained unchanged during catalytic reduction of the nitro function, and it was revealed by HCl elimination at a later stage. The 1-deazapurine I and the tricyclic derivative II have been prepared

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(25) OF 42 COMPOSED OF RX(3), RX(4), RX(8)
RX(25) 2 K + H + AC ===> AD




```
RX(3)     RCT  K 107-07-3
          RGT  M 7791-25-5 SO2Cl2
          PRO  L 5411-48-3
          SOL  75-09-2 CH2Cl2
          CON  2 hours, 0 deg C

RX(4)     RCT  H 5709-48-8, L 5411-48-3

            STAGE(1)
               CON  2 hours, 100 deg C

            STAGE(2)
               RGT  D 7664-93-9 H2SO4
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 2 hours, reflux
                    SUBSTAGE(2) cooled

            STAGE(3)
               RGT  P 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  0 deg C, pH 11
```

```
          PRO  O 13182-80-4
          NTE  no solvent in stage 1

RX(8)     RCT  O 13182-80-4

            STAGE(1)
               RGT  W 1333-74-0 H2
               CAT  7440-05-3 Pd
               SOL  123-91-1 Dioxane
               CON  room temperature, 1 atm

            STAGE(2)
               RCT  AC 123-06-8
               SOL  123-91-1 Dioxane
               CON  overnight, room temperature

          PRO  AD 810660-39-0


RX(34) OF 42 COMPOSED OF REACTION SEQUENCE RX(3), RX(4), RX(8)
               AND REACTION SEQUENCE RX(2), RX(4), RX(8)
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...  A  +  F  +  G  +  L  +  AC  ===>  AD
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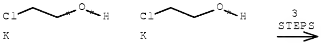
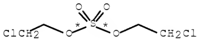
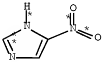


K K



L

START NEXT REACTION SEQUENCE



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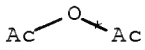

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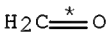

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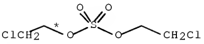

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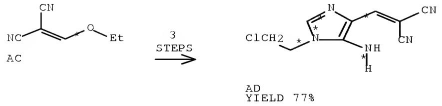


```
RX(3)     RCT  K 107-07-3
          RGT  M 7791-25-5 SO2Cl2
          PRO  L 5411-48-3
          SOL  75-09-2 CH2Cl2
          CON  2 hours, 0 deg C

RX(2)     RCT  A 3034-38-6, F 108-24-7, G 50-00-0
          PRO  H 5709-48-8
          CAT  127-09-3 AcONa
          SOL  108-88-3 PhMe
          CON  90 hours, 100 deg C
          NTE  paraformaldehyde used

RX(4)     RCT  H 5709-48-8, L 5411-48-3

            STAGE(1)
               CON  2 hours, 100 deg C

            STAGE(2)
               RGT  D 7664-93-9 H2SO4
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 2 hours, reflux
                    SUBSTAGE(2) cooled

            STAGE(3)
               RGT  P 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  0 deg C, pH 11

          PRO  O 13182-80-4
          NTE  no solvent in stage 1

RX(8)     RCT  O 13182-80-4

            STAGE(1)
               RGT  W 1333-74-0 H2
               CAT  7440-05-3 Pd
               SOL  123-91-1 Dioxane
               CON  room temperature, 1 atm

            STAGE(2)
               RCT  AC 123-06-8
               SOL  123-91-1 Dioxane
               CON  overnight, room temperature

          PRO  AD 810660-39-0
```

L48 ANSWER 6 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	139:85383 CASREACT Full-text
TITLE:	Preparation of pyridoquinoxaline derivatives as antiviral agents
INVENTOR(S):	Strohbach, Joseph W.; Tanis, Steven P.; Moon, Malcolm W.; Perrault, William R.
PATENT ASSIGNEE(S):	Pharmacia & Upjohn Company, USA
SOURCE:	PCT Int. Appl., 31 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053972	A1	20030703	WO 2002-US37614	20021219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473862	A1	20030703	CA 2002-2473862	20021219
AU 2002352882	A1	20030709	AU 2002-352882	20021219
US 20030130255	A1	20030710	US 2002-325248	20021219
US 6686356	B2	20040203		
EP 1456208	A1	20040915	EP 2002-789842	20021219
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BR 2002015067	A	20041109	BR 2002-15067	20021219
JP 2005516957	T	20050609	JP 2003-554688	20021219
US 20040106596	A1	20040603	US 2003-721119	20031125
MX 2004PA06030	A	20040927	MX 2004-PA6030	20040618
PRIORITY APPLN. INFO.:			US 2001-342874P	20011220
			US 2002-325248	20021219
			WO 2002-US37614	20021219

OTHER SOURCE(S): MARPAT 139:85383

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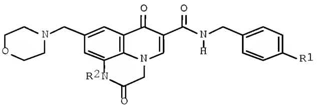
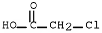


I

AB The present invention provides a synthesis of pyridoquinoxaline derivs. I (R1 = F, Cl, Br, cyano, NO2, R2 = alkyl, substituted alkyl, arylalkyl, etc.) to be used as antiviral agents. Thus, I (R1 = Cl, R2 = Me) was prepared by two methods, both starting from 3-fluoro-4-nitrotoluene (II). Thus, II was brominated and reacted with morpholine to give 4-(3-fluoro-4-nitrobenzyl)morpholine, which was converted to N-methyl-5-(morpholin-4-ylmethyl)-2-nitroaniline. The latter compound was then converted to I (R1 = Cl, R2 = Me) in 4 steps. The compds. are intended to be used as antiviral agents to treat human herpesviruses, human simplex viruses, and cytomegalovirus. They can be administered orally, parenterally, or topically. These compds. are also designed to inhibit DNA polymerase and treat atherosclerosis and restenosis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(12) OF 63 ...AG + O ===> AH...



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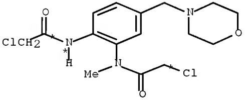

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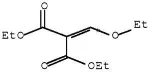

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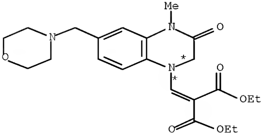


AH

```
RX(12)    RCT  AG 552884-01-2

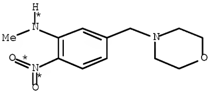
            STAGE(1)
               RGT  AI 1310-73-2 NaOH
               SOL  7732-18-5 Water, 109-99-9 THF
               CON  SUBSTAGE(1) 13 - 17 deg C
                    SUBSTAGE(2) 20 minutes

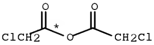
            STAGE(2)
               RGT  AJ 12125-02-9 NH4Cl
               SOL  7732-18-5 Water, 108-88-3 PhMe

            STAGE(3)
               RCT  O 87-13-8
               CON  SUBSTAGE(2) 123 deg C
                    SUBSTAGE(3) 3 hours, 122 - 125 deg C

          PRO  AH 552884-02-3
          NTE  Isopar-H present in last stage


RX(24) OF 63 COMPOSED OF RX(11), RX(12)
RX(24)    AC  +  3 AF  +  O  ===>  AH
```


AC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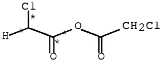
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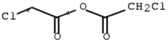
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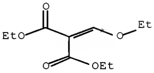
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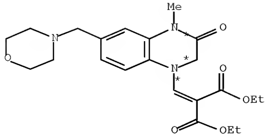


AH

RX(11) RCT AC 552883-99-5

STAGE(1)
RGT L 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 109-99-9 THF
CON 1 hour, 14 deg C

STAGE(2)
RCT AF 541-88-8
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 deg C
SUBSTAGE(2) 30 minutes, 8 - 11 deg C
SUBSTAGE(3) 30 minutes

PRO AG 552884-01-2

RX(12) RCT AG 552884-01-2

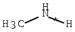
STAGE(1)
RGT AI 1310-73-2 NaOH
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 13 - 17 deg C
SUBSTAGE(2) 20 minutes

STAGE(2)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 108-88-3 PhMe

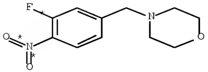
STAGE(3)
RCT O 87-13-8
CON SUBSTAGE(2) 123 deg C
SUBSTAGE(3) 3 hours, 122 - 125 deg C

PRO AH 552884-02-3
NTE Isopar-H present in last stage

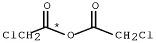
RX(42) OF 63 COMPOSED OF RX(10), RX(11), RX(12)
RX(42) AB + F + 3 AF + O ===> AH



AB



F



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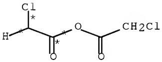

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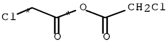

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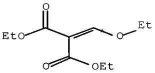

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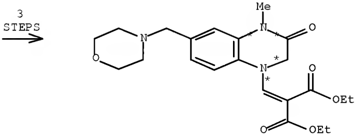


AH

```
RX(10)    RCT  AB 74-89-5, F 552883-91-7

            STAGE(1)
               SOL  7732-18-5 Water, 67-68-5 DMSO
               CON  SUBSTAGE(2) 30 minutes
                    SUBSTAGE(3) 5 minutes, 47 deg C
                    SUBSTAGE(4) <51 deg C
                    SUBSTAGE(5) 45 minutes, 50 deg C

            STAGE(2)
               SOL  7732-18-5 Water

          PRO  AC 552883-99-5

RX(11)    RCT  AC 552883-99-5

            STAGE(1)
               RGT  L 1333-74-0 H2
               CAT  7440-05-3 Pd
               SOL  109-99-9 THF
```

CON 1 hour, 14 deg C

STAGE(2)
RCT AF 541-88-8
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 deg C
SUBSTAGE(2) 30 minutes, 8 - 11 deg C
SUBSTAGE(3) 30 minutes

PRO AG 552884-01-2

RX(12) RCT AG 552884-01-2

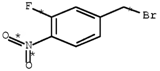
STAGE(1)
RGT AI 1310-73-2 NaOH
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 13 - 17 deg C
SUBSTAGE(2) 20 minutes

STAGE(2)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(3)
RCT O 87-13-8
CON SUBSTAGE(2) 123 deg C
SUBSTAGE(3) 3 hours, 122 - 125 deg C

PRO AH 552884-02-3
NTE Isopar-H present in last stage

RX(43) OF 63 COMPOSED OF RX(2), RX(10), RX(11), RX(12)
RX(43) B + E + AB + 3 AF + O ===> AH



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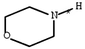

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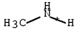
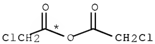


AB



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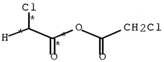

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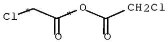

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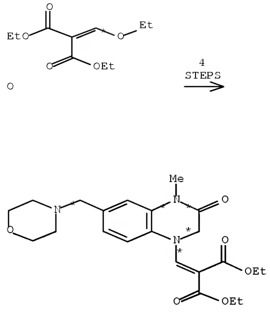


AH

```
RX(2)      RCT  B 131858-37-2, E 110-91-8
           PRO  F 552883-91-7
           SOL  109-99-9 THF
           CON  SUBSTAGE(1) room temperature
                SUBSTAGE(2) 1 hour, room temperature

RX(10)     RCT  AB 74-89-5, F 552883-91-7

             STAGE(1)
                SOL  7732-18-5 Water, 67-68-5 DMSO
                CON  SUBSTAGE(2) 30 minutes
                     SUBSTAGE(3) 5 minutes, 47 deg C
                     SUBSTAGE(4) <51 deg C
                     SUBSTAGE(5) 45 minutes, 50 deg C

             STAGE(2)
                SOL  7732-18-5 Water

           PRO  AC 552883-99-5

RX(11)     RCT  AC 552883-99-5

             STAGE(1)
                RGT  L 1333-74-0 H2
                CAT  7440-05-3 Pd
                SOL  109-99-9 THF
                CON  1 hour, 14 deg C

             STAGE(2)
                RCT  AF 541-88-8
                SOL  109-99-9 THF
                CON  SUBSTAGE(1) 10 deg C
                     SUBSTAGE(2) 30 minutes, 8 - 11 deg C
```

```
                    SUBSTAGE(3) 30 minutes

          PRO  AG 552884-01-2

RX(12)    RCT  AG 552884-01-2

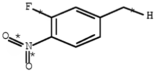
            STAGE(1)
               RGT  AI 1310-73-2 NaOH
               SOL  7732-18-5 Water, 109-99-9 THF
               CON  SUBSTAGE(1) 13 - 17 deg C
                    SUBSTAGE(2) 20 minutes

            STAGE(2)
               RGT  AJ 12125-02-9 NH4Cl
               SOL  7732-18-5 Water, 108-88-3 PhMe

            STAGE(3)
               RCT  O 87-13-8
               CON  SUBSTAGE(2) 123 deg C
                    SUBSTAGE(3) 3 hours, 122 - 125 deg C

          PRO  AH 552884-02-3
          NTE  Isopar-H present in last stage


RX(47) OF 63 COMPOSED OF RX(1), RX(2), RX(10), RX(11), RX(12)
RX(47)    A  +  E  +  AB  +  3 AF  +  O  ===>  AH
```



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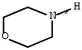

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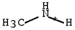
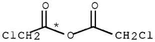


AB



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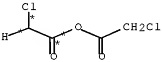

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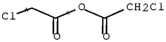

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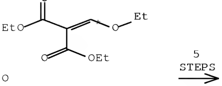

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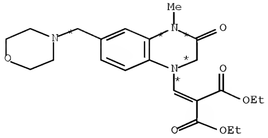


AH

RX(1) RCT A 446-34-4
RGT C 128-08-5 Bromosuccinimide
PRO B 131858-37-2
SOL 107-06-2 ClCH2CH2Cl
CON SUBSTAGE(1) 1 hour, 0 - 25 deg C
SUBSTAGE(3) 15 minutes
NTE photochem.

RX(2) RCT B 131858-37-2, E 110-91-8
PRO F 552883-91-7
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(10) RCT AB 74-89-5, F 552883-91-7

STAGE(1)
SOL 7732-18-5 Water, 67-68-5 DMSO
CON SUBSTAGE(2) 30 minutes
SUBSTAGE(3) 5 minutes, 47 deg C
SUBSTAGE(4) <51 deg C
SUBSTAGE(5) 45 minutes, 50 deg C

STAGE(2)
SOL 7732-18-5 Water

PRO AC 552883-99-5

RX(11) RCT AC 552883-99-5

STAGE(1)
RGT L 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 109-99-9 THF
CON 1 hour, 14 deg C

STAGE(2)
RCT AF 541-88-8
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 deg C
SUBSTAGE(2) 30 minutes, 8 - 11 deg C

```
                SUBSTAGE(3) 30 minutes

        PRO  AG 552884-01-2

RX(12)  RCT  AG 552884-01-2

          STAGE(1)
             RGT  AI 1310-73-2 NaOH
             SOL  7732-18-5 Water, 109-99-9 THF
             CON  SUBSTAGE(1) 13 - 17 deg C
                  SUBSTAGE(2) 20 minutes

          STAGE(2)
             RGT  AJ 12125-02-9 NH4Cl
             SOL  7732-18-5 Water, 108-88-3 PhMe

          STAGE(3)
             RCT  O 87-13-8
             CON  SUBSTAGE(2) 123 deg C
                  SUBSTAGE(3) 3 hours, 122 - 125 deg C

        PRO  AH 552884-02-3
        NTE  Isopar-H present in last stage
```

L48 ANSWER 7 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 139:52960 CASREACT Full-text

TITLE: Synthesis and antiinflammatory activity of novel indazolones

AUTHOR(S): Abouzid, Khaled A. M.; El-Abhar, H. S.

CORPORATE SOURCE: Pharmaceutical Chemistry Department, Faculty of Pharmacy, Ain-Shams University, Cairo, 11566, Egypt

SOURCE: Archives of Pharmacal Research (2003), 26(1), 1-8
CODEN: APHRDQ; ISSN: 0253-6269

PUBLISHER: Pharmaceutical Society of Korea

DOCUMENT TYPE: Journal

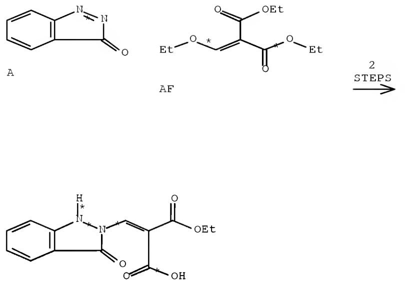
LANGUAGE: English

AB In this study, a series of new N2-substituted 1,2-dihydro-3H-indazol-3- ones as well as their condensed pyrazolo, pyridazino derivs. such as pyridazino[1,2-a]indazole-6,9,11-triones and 3,9-dioxo-3H,9H-pyrazolo[1,2-a]indazole were synthesized. The antiinflammatory activity of some synthesized compds. was determined by carrageenan-induced rat paw edema technique using diclofenac as reference drug. The pharmacol. data showed that most of the tested compds. exhibited a significant long lasting antiinflammatory activity, which in the case of γ,3-dioxo-α-[(trifluoroacetyl)amino]-2H-Indazole-2-butanoic acid was superior to that of diclofenac.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(26) OF 35 COMPOSED OF RX(17), RX(18)

RX(26) A + AF ===> AJ



AJ
YIELD 37%

RX(17) RCT A 5686-93-1, AF 87-13-8
PRO AI 545444-13-1
SOL 60-29-7 Et2O
CON 6 hours, 170 deg C

RX(18) RCT AI 545444-13-1

STAGE(1)
RGT AK 1310-73-2 NaOH
SOL 7732-18-5 Water
CON 2 hours, room temperature

STAGE(2)
RGT AL 7647-01-0 HCl
SOL 7732-18-5 Water

PRO AJ 545444-14-2

L48 ANSWER 8 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

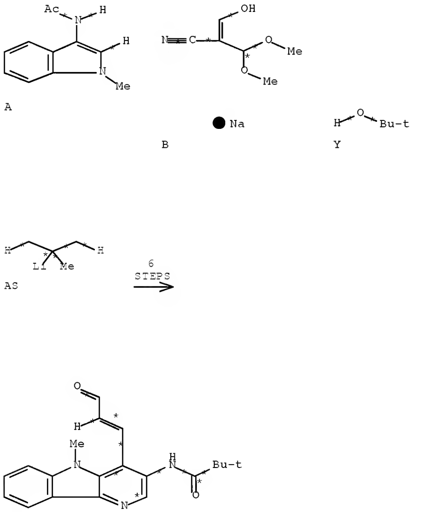
ACCESSION NUMBER:	135:210953 CASREACT Full-text
TITLE:	A convenient synthesis of 3,4-difunctionalized δ-carbolines
AUTHOR(S):	Papamicael, C.; Queguiner, G.; Bourguignon, J.; Dupas, G.
CORPORATE SOURCE:	Laboratoire de Chimie Organique Fine et Heterocyclique, UPRESA 6014, INSA-IRCOF, Mont-Saint-Aignan, 76131, Fr.
SOURCE:	Tetrahedron (2001), 57(25), 5385-5391 CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER:	Elsevier Science Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB An efficient and direct preparation of functionalized δ-carbolines, via a ring closure reaction between the appropriate indole amine and a masked 1,3-dicarbonyl compound is described. This method afforded new 3-substituted δ-carbolines and these products were subjected to ortho-lithiation expts. Various 3,4-disubstituted δ-carbolines were obtained in acceptable yields.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(89) OF 95 COMPOSED OF RX(1), RX(3), RX(4), RX(7), RX(8), RX(17)

RX(89) A + B + Y + AS ===> AW



A

B

Y

AS

AW
YIELD 35%

RX(1) RCT A 85729-26-6, B 105161-33-9
RGT D 7647-01-0 HCl
PRO C 358332-93-1
SOL 67-56-1 MeOH, 7732-18-5 Water

```
RX(3)      RCT  C 358332-93-1

             STAGE(1)
                RGT  K 1310-73-2 NaOH, L 7722-84-1 H2O2
                SOL  64-17-5 EtOH, 7732-18-5 Water

             STAGE(2)
                RGT  M 7664-93-9 H2SO4
                SOL  7732-18-5 Water

           PRO  J 358332-94-2

RX(4)      RCT  J 358332-94-2

             STAGE(1)
                RGT  K 1310-73-2 NaOH
                SOL  64-17-5 EtOH

             STAGE(2)
                RGT  D 7647-01-0 HCl
                SOL  7732-18-5 Water

           PRO  O 358332-95-3

RX(7)      RCT  O 358332-95-3, Y 75-65-0
           RGT  AA 26386-88-9 (PhO)2P(O)N3, AB 121-44-8 Et3N
           PRO  Z 358332-98-6
           SOL  75-65-0 t-BuOH

RX(8)      RCT  Z 358332-98-6

             STAGE(1)
                RGT  M 7664-93-9 H2SO4
                SOL  7732-18-5 Water

             STAGE(2)
                RGT  AB 121-44-8 Et3N, AD 3282-30-2 Pivaloyl chloride
                SOL  109-99-9 THF

           PRO  AC 358332-99-7

RX(17)     RCT  AC 358332-99-7

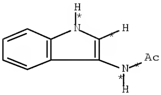
             STAGE(1)
                RGT  AR 110-18-9 TMEDA
                SOL  109-99-9 THF

             STAGE(2)
                RCT  AS 594-19-4
                SOL  109-66-0 Pentane

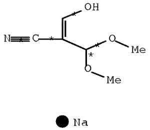
             STAGE(3)
                RGT  AN 109-94-4 HCO2Et

           PRO  AW 358333-10-5
           NTE  stereoselective


RX(94) OF 95 COMPOSED OF RX(2), RX(3), RX(4), RX(7), RX(8), RX(17)
RX(94)     G  +  B  +  H  +  Y  +  AS  ===>  AW
```



G



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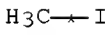

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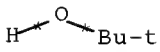
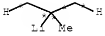
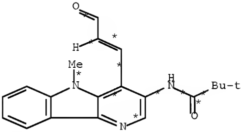


Y



AS

6
STEPS



AW
YIELD 35%

```
RX(2)      RCT  G 51030-59-2, B 105161-33-9

             STAGE(1)
                RGT  D 7647-01-0 HCl
                SOL  67-56-1 MeOH, 7732-18-5 Water

             STAGE(2)
                RCT  H 74-88-4
                RGT  I 7646-69-7 NaH

           PRO  C 358332-93-1

RX(3)      RCT  C 358332-93-1

             STAGE(1)
                RGT  K 1310-73-2 NaOH, L 7722-84-1 H2O2
```

```
              SOL  64-17-5 EtOH, 7732-18-5 Water

           STAGE(2)
              RGT  M 7664-93-9 H2SO4
              SOL  7732-18-5 Water

         PRO  J 358332-94-2

RX(4)    RCT  J 358332-94-2

           STAGE(1)
              RGT  K 1310-73-2 NaOH
              SOL  64-17-5 EtOH

           STAGE(2)
              RGT  D 7647-01-0 HCl
              SOL  7732-18-5 Water

         PRO  O 358332-95-3

RX(7)    RCT  O 358332-95-3, Y 75-65-0
         RGT  AA 26386-88-9 (PhO)2P(O)N3, AB 121-44-8 Et3N
         PRO  Z 358332-98-6
         SOL  75-65-0 t-BuOH

RX(8)    RCT  Z 358332-98-6

           STAGE(1)
              RGT  M 7664-93-9 H2SO4
              SOL  7732-18-5 Water

           STAGE(2)
              RGT  AB 121-44-8 Et3N, AD 3282-30-2 Pivaloyl chloride
              SOL  109-99-9 THF

         PRO  AC 358332-99-7

RX(17)   RCT  AC 358332-99-7

           STAGE(1)
              RGT  AR 110-18-9 TMEDA
              SOL  109-99-9 THF

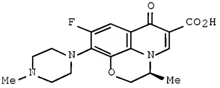
           STAGE(2)
              RCT  AS 594-19-4
              SOL  109-66-0 Pentane

           STAGE(3)
              RGT  AN 109-94-4 HCO2Et

         PRO  AW 358333-10-5
         NTE  stereoselective

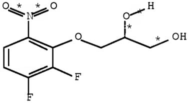

L48  ANSWER 9 OF 16  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        132:22935  CASREACT  Full-text
TITLE:                   A practical stereoselective synthesis of
                         (S)-(-)-ofloxacin
AUTHOR(S):               Yang, Yu-She; Ji, Ru-Yun; Chen, Kai-Xian
CORPORATE SOURCE:        Shanghai Institute of Materia Medica, Chinese Academy
```

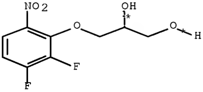
of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (1999), 17(5), 539-544
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

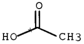

I

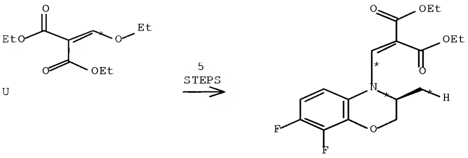
AB A very efficient and practical procedure for preparation of (S)-(-)-ofloxacin (I) has been developed (10 steps, overall yield ≥45%). The key step of this approach is the regioselective nucleophilic substitution of 2-position fluorine atom of 2,3,4-trifluoronitrobenzene by (S)-glycerol acetonide.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(38) OF 55 COMPOSED OF RX(3), RX(4), RX(5), RX(6), RX(7)
RX(38) 2 G + 2 J + U ===> W


G


G


2 J



W
YIELD 95%

```
RX(3)      RCT  G 251945-87-6, J 64-19-7
           RGT  M 10035-10-6 HBr
           PRO  K 251945-88-7, L 251945-89-8
           NTE  98% overall yield

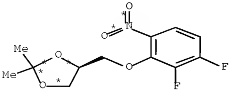
RX(4)      RCT  K 251945-88-7, L 251945-89-8
           RGT  O 1310-73-2 NaOH
           PRO  N 132027-28-2
           SOL  7732-18-5 Water
           NTE  stereoselective synthesis

RX(5)      RCT  N 132027-28-2
           RGT  R 1333-74-0 H2
           PRO  Q 124409-98-9
           CAT  7440-05-3 Pd, 7440-44-0 Carbon
           SOL  64-17-5 EtOH
           NTE  stereoselective synthesis

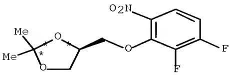
RX(6)      RCT  Q 124409-98-9, U 87-13-8
           PRO  V 124532-06-5
           NTE  heated 145-150

RX(7)      RCT  V 124532-06-5
           RGT  X 1972-28-7 EtO2CN:NCO2Et, Y 603-35-0 PPh3
           PRO  W 106939-43-9
           SOL  109-99-9 THF
           NTE  stereoselective synthesis

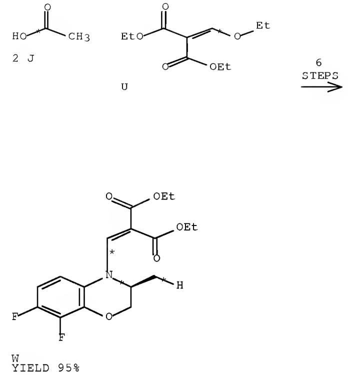

RX(39) OF 55 COMPOSED OF RX(2), RX(3), RX(4), RX(5), RX(6), RX(7)
RX(39)     2 C  +  2 J  +  U  ===>  W
```



C



C



RX(2) RCT C 251945-86-5
RGT H 7647-01-0 HCl
PRO G 251945-87-6
SOL 64-17-5 EtOH
NTE stereoselective synthesis

RX(3) RCT G 251945-87-6, J 64-19-7
RGT M 10035-10-6 HBr
PRO K 251945-88-7, L 251945-89-8
NTE 98% overall yield

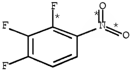
RX(4) RCT K 251945-88-7, L 251945-89-8
RGT O 1310-73-2 NaOH
PRO N 132027-28-2
SOL 7732-18-5 Water
NTE stereoselective synthesis

RX(5) RCT N 132027-28-2
RGT R 1333-74-0 H2
PRO Q 124409-98-9
CAT 7440-05-3 Pd, 7440-44-0 Carbon
SOL 64-17-5 EtOH
NTE stereoselective synthesis

RX(6) RCT Q 124409-98-9, U 87-13-8
PRO V 124532-06-5
NTE heated 145-150

```
RX(7)      RCT  V 124532-06-5
           RGT  X 1972-28-7 EtO2CN:NCO2Et, Y 603-35-0 PPh3
           PRO  W 106939-43-9
           SOL  109-99-9 THF
           NTE  stereoselective synthesis


RX(40) OF 55 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5), RX(6), RX(7)
RX(40)     2 A  +  2 B  +  2 J  +  U  ===>
           W
```



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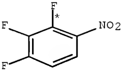

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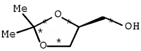

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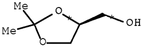

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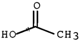
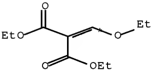
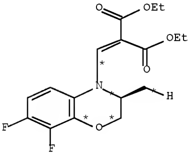


2 J



U

7
STEPS



W
YIELD 95%

```
RX(1)      RCT  A 771-69-7

             STAGE(1)
                RGT  D 1310-58-3 KOH, E 584-08-7 K2CO3
                SOL  108-88-3 PhMe
```

```
            STAGE(2)
               RCT  B 22323-82-6

         PRO  C 251945-86-5

RX(2)    RCT  C 251945-86-5
         RGT  H 7647-01-0 HCl
         PRO  G 251945-87-6
         SOL  64-17-5 EtOH
         NTE  stereoselective synthesis

RX(3)    RCT  G 251945-87-6, J 64-19-7
         RGT  M 10035-10-6 HBr
         PRO  K 251945-88-7, L 251945-89-8
         NTE  98% overall yield

RX(4)    RCT  K 251945-88-7, L 251945-89-8
         RGT  O 1310-73-2 NaOH
         PRO  N 132027-28-2
         SOL  7732-18-5 Water
         NTE  stereoselective synthesis

RX(5)    RCT  N 132027-28-2
         RGT  R 1333-74-0 H2
         PRO  Q 124409-98-9
         CAT  7440-05-3 Pd, 7440-44-0 Carbon
         SOL  64-17-5 EtOH
         NTE  stereoselective synthesis

RX(6)    RCT  Q 124409-98-9, U 87-13-8
         PRO  V 124532-06-5
         NTE  heated 145-150

RX(7)    RCT  V 124532-06-5
         RGT  X 1972-28-7 EtO2CN:NCO2Et, Y 603-35-0 PPh3
         PRO  W 106939-43-9
         SOL  109-99-9 THF
         NTE  stereoselective synthesis
```

L48 ANSWER 10 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 131:214260 CASREACT Full-text

TITLE: An efficient synthesis of ofloxacin and levofloxacin from 3,4-difluoroaniline

AUTHOR(S): Adrio, Javier; Carretero, Juan C.; Ruano, Jose L. Garcia; Pallares, Antonio; Vicioso, Mercedes

CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Ciencias, Universidad Autonoma de Madrid, Madrid, 28049, Spain

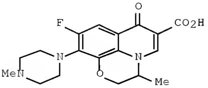
SOURCE: Heterocycles (1999), 51(7), 1563-1572
CODEN: HTCYAM; ISSN: 0385-5414

PUBLISHER: Japan Institute of Heterocyclic Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

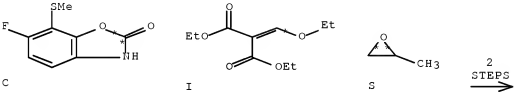


I

AB The functionalization at either C-2 or C-3 of N-(tert-butoxycarbonyl)-3,4-difluoroaniline, based on its ortho-deprotonation under different exptl. conditions, is described. This process can be readily applied to the synthesis of ofloxacin [(±)-I], levofloxacin [(S)-I], and related compds.

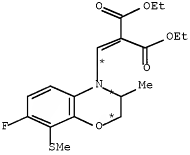
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(15) OF 34 COMPOSED OF RX(2), RX(6)
RX(15) C + I + S ===> T



C I S

2 STEPS



T
YIELD 41%

RX(2) RCT C 243448-03-5

STAGE(1)
RGT K 1310-58-3 KOH
SOL 7732-18-5 Water, 64-17-5 EtOH

STAGE(2)

```
            RGT   E 7647-01-0 HCl
            SOL   7732-18-5 Water

         STAGE(3)
            RCT   I 87-13-8

         STAGE(4)
            SOL   110-54-3 Hexane

       PRO   J 243448-07-9
       NTE   intermediate adduct was isolated

RX(6)  RCT   J 243448-07-9

         STAGE(1)
            RGT   U 7791-03-9 LiClO4
            CAT   7646-69-7 NaH
            SOL   109-99-9 THF

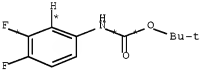
         STAGE(2)
            RCT   S 75-56-9

         STAGE(3)
            RGT   H 7732-18-5 Water

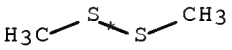
         STAGE(4)
            RGT   V 603-35-0 PPh3, W 1972-28-7 EtO2CN:NCO2Et
            SOL   109-99-9 THF

       PRO   T 243448-08-0
       NTE   intermediate adduct was isolated

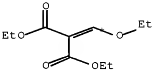

RX(22) OF 34 COMPOSED OF RX(1), RX(2), RX(6)
RX(22)    A  +  B  +  I  +  S  ===>  T
```



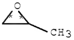
A



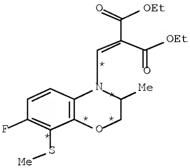
B



I



S



T
YIELD 41%

```
RX(1)      RCT  A 144298-04-4

             STAGE(1)
                RGT  D 594-19-4 t-BuLi
                SOL  109-99-9 THF, 110-54-3 Hexane

             STAGE(2)
                RCT  B 624-92-0

             STAGE(3)
                RGT  E 7647-01-0 HCl
                SOL  7732-18-5 Water

           PRO  C 243448-03-5
           NTE  reaction temp. dets. product

RX(2)      RCT  C 243448-03-5

             STAGE(1)
                RGT  K 1310-58-3 KOH
                SOL  7732-18-5 Water, 64-17-5 EtOH

             STAGE(2)
                RGT  E 7647-01-0 HCl
                SOL  7732-18-5 Water

             STAGE(3)
                RCT  I 87-13-8

             STAGE(4)
                SOL  110-54-3 Hexane

           PRO  J 243448-07-9
           NTE  intermediate adduct was isolated

RX(6)      RCT  J 243448-07-9

             STAGE(1)
                RGT  U 7791-03-9 LiClO4
                CAT  7646-69-7 NaH
                SOL  109-99-9 THF
```

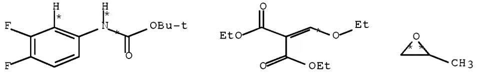
STAGE(2)
RCT S 75-56-9

STAGE(3)
RGT H 7732-18-5 Water

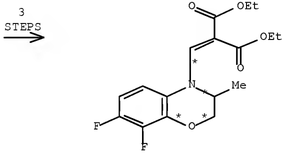
STAGE(4)
RGT V 603-35-0 PPh3, W 1972-28-7 EtO2CN:NCO2Et
SOL 109-99-9 THF

PRO T 243448-08-0
NTE intermediate adduct was isolated

RX(31) OF 34 COMPOSED OF RX(11), RX(10), RX(12)
RX(31) A + I + S ===> AN



A I S



AN
YIELD 76%

RX(11) RCT A 144298-04-4

STAGE(1)
RGT D 594-19-4 t-BuLi
SOL 109-99-9 THF, 109-66-0 Pentane

STAGE(2)
RGT AK 121-43-7 Me borate

STAGE(3)
RGT AL 7722-84-1 H2O2
SOL 64-19-7 AcOH, 7732-18-5 Water

```
          STAGE(4)
             RGT  E 7647-01-0 HCl

        PRO  AI 115551-33-2

RX(10)  RCT  AI 115551-33-2, I 87-13-8
        PRO  AJ 85741-74-8
        SOL  64-17-5 EtOH

RX(12)  RCT  AJ 85741-74-8

          STAGE(1)
             RGT  U 7791-03-9 LiClO4
             CAT  7646-69-7 NaH
             SOL  109-99-9 THF

          STAGE(2)
             RCT  S 75-56-9

          STAGE(3)
             RGT  H 7732-18-5 Water

          STAGE(4)
             RGT  V 603-35-0 PPh3, W 1972-28-7 EtO2CN:NCO2Et
             SOL  109-99-9 THF

        PRO  AN 86760-99-8
        NTE  S-analog similarly prepd.,  intermediate adduct was isolated


L48  ANSWER 11 OF 16  CASREACT  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        121:9414  CASREACT  Full-text
TITLE:                   Process for obtaining benzoxazines useful for the
                         synthesis of ofloxacin, levofloxacin and derivatives
INVENTOR(S):             Carretero Gonzalvez, Juan Carlo; Vicioso Sanchez,
                         Mercedes; Garcia Ruano, Jose Luis
PATENT ASSIGNEE(S):      Derivados del Etilo, S.A., Spain
SOURCE:                  PCT Int. Appl., 30 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                Spanish
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

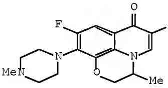
     PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
     ---------------     ----  --------      ---------------   --------
     WO 9407873           A1   19940414      WO 1993-ES80      19931006
         W:  AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, FI, GB, HU, JP, KP, KR,
             LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA,
             US, VN
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
             BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
     ES 2055656           A1   19940816      ES 1992-1983      19921007
     ES 2055656           B1   19951116
     ES 2069500           A1   19950501      ES 1993-2080      19931004
     ES 2069500           B1   19960301
     AU 9351118           A    19940426      AU 1993-51118     19931006
     AU 674542            B2   19970102
     EP 619311            A1   19941012      EP 1993-921930    19931006
```

R: AT, BE, CH, DE, DK, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

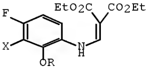
JP 07501835	T	19950223	JP 1993-508738	19931006
KR 131914	B1	19980417	KR 1994-701925	19940607
ZA 9405098	A	19950222	ZA 1994-5098	19940713
US 5521310	A	19960528	US 1994-244455	19940831
AU 9665878	A	19961212	AU 1996-65878	19960927
AU 686955	B2	19980212		
PRIORITY APPLN. INFO.:			ES 1992-1983	19921007
			ES 1993-2080	19931004
			WO 1993-ES80	19931006

OTHER SOURCE(S): MARPAT 121:9414

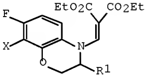
GI



I



II

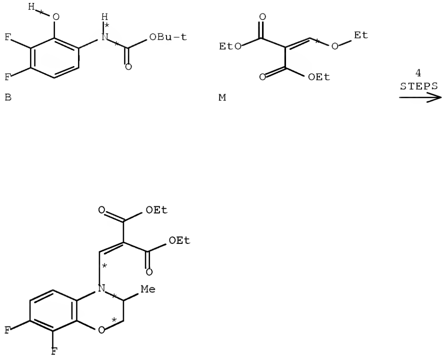


III

AB The antimicrobial agents ofloxacin [(±)-I], levofloxacin [(S)-I], and their derivs. and analogs are prepared in several steps. via (anilinomethylene)malonates II [R = H, CH2CH(OH)R1; R1 = H, C1-6 alkyl (especially Me), C2-6 alkenyl, aryl; X = halo (especially F)] and benzoxazines III. For example, 3,4-difluoroaniline underwent N-tert-butoxycarbonylation (98-99%), lithiation and hydroxylation in the 2-position (89%), N-deprotection (86%), and condensation with di-Et (ethoxymethylene)malonate (80-81%) to give II [R = H, X = F]. Treatment of this with NaH, LiClO4, and propylene oxide in THF gave 65% II [R = CH2CH(OH)Me, X = F], which was cyclized by PPh3 and di-Et azodicarboxylate (79%) to give III [R1 = Me, X = F]. Cyclization of the latter by AcOH-H2SO4 (73%), saponification by HCl-AcOH (68%), and condensation with N-methylpiperazine (79%) gave (±)-I. By using the appropriate chiral epoxide, and proceeding via enantiomeric intermediates, enantiomeric products such as (S)-I may be obtained without resolution (claimed, no examples).

RX(26) OF 48 COMPOSED OF RX(2), RX(3), RX(4), RX(5)

RX(26) B + M ===> R



R
YIELD 79%

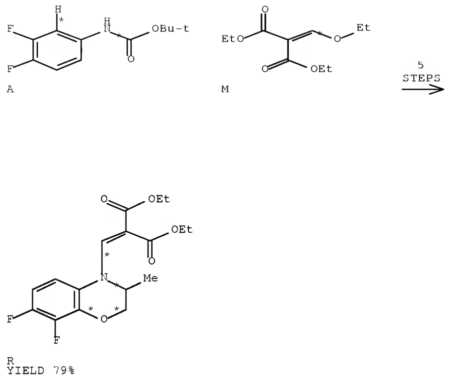
RX(2)　RCT B 155537-32-9
RGT K 7647-01-0 HCl
PRO J 115551-33-2
SOL 60-29-7 Et2O, 7732-18-5 Water
NTE room temp.

RX(3)　RCT J 115551-33-2, M 87-13-8
PRO N 85741-74-8
NTE neat, 110°

RX(4)　RCT N 85741-74-8
RGT P 7646-69-7 NaH
PRO O 124409-86-5
CAT 7791-03-9 LiClO4
SOL 109-99-9 THF
NTE 40°

RX(5)　RCT O 124409-86-5
RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et
PRO R 86760-99-8
SOL 109-99-9 THF
NTE room temp.

RX(34) OF 48 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5)
RX(34) A + M ===> P



RX(1) RCT A 144298-04-4

STAGE(1)
RGT C 109-72-8 BuLi
SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)
RGT D 121-43-7 Me borate

STAGE(3)
RGT E 64-19-7 AcOH, F 7722-84-1 H2O2
SOL 7732-18-5 Water

PRO B 155537-32-9
NTE -78° to room temp.

RX(2) RCT B 155537-32-9
RGT K 7647-01-0 HCl
PRO J 115551-33-2
SOL 60-29-7 Et2O, 7732-18-5 Water
NTE room temp.

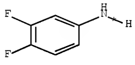
RX(3) RCT J 115551-33-2, M 87-13-8
PRO N 85741-74-8
NTE neat, 110°

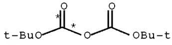
RX(4) RCT N 85741-74-8
RGT P 7646-69-7 NaH
PRO O 124409-86-5
CAT 7791-03-9 LiClO4

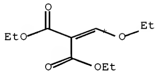
SOL 109-99-9 THF
NTE 40°

RX(5) RCT O 124409-86-5
RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et
PRO R 86760-99-8
SOL 109-99-9 THF
NTE room temp.

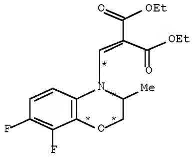
RX(36) OF 48 COMPOSED OF RX(10), RX(1), RX(2), RX(3), RX(4), RX(5)
RX(36) AE + AF + M ===> R


AE


AF


M

6
STEPS
→


R
YIELD 79%

RX(10) RCT AE 3863-11-4, AF 24424-99-5
PRO A 144298-04-4
SOL 109-99-9 THF
NTE 60°

RX(1) RCT A 144298-04-4

STAGE(1)
RGT C 109-72-8 BuLi

SOL 109-99-9 THF, 110-54-3 Hexane

STAGE(2)
RGT D 121-43-7 Me borate

STAGE(3)
RGT E 64-19-7 AcOH, F 7722-84-1 H2O2
SOL 7732-18-5 Water

PRO B 155537-32-9
NTE -78° to room temp.

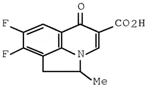
RX(2) RCT B 155537-32-9
RGT K 7647-01-0 HCl
PRO J 115551-33-2
SOL 60-29-7 Et2O, 7732-18-5 Water
NTE room temp.

RX(3) RCT J 115551-33-2, M 87-13-8
PRO N 85741-74-8
NTE neat, 110°

RX(4) RCT N 85741-74-8
RGT P 7646-69-7 NaH
PRO O 124409-86-5
CAT 7791-03-9 LiClO4
SOL 109-99-9 THF
NTE 40°

RX(5) RCT O 124409-86-5
RGT S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et
PRO R 86760-99-8
SOL 109-99-9 THF
NTE room temp.

L48 ANSWER 12 OF 16 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 111:23362 CASREACT Full-text
TITLE: Synthesis of 8,9-difluoro-2-methyl-6-oxo-1,2-dihydropyrrolo[3,2,1-ij]quinoline-5-carboxylic acid
AUTHOR(S): Parikh, Vinod D.; Fray, Andrew H.; Kleinman, Edward F.
CORPORATE SOURCE: Dep. Med. Chem., Pfizer Cent. Res., Groton, CT, 06340, USA
SOURCE: Journal of Heterocyclic Chemistry (1988), 25(5), 1567-9
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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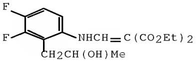
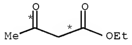


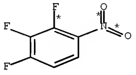
II

AB The arylation of MeCOCH2CO2Et by 2,3,4-F3C6H2NO2 and subsequent hydrolysis-decarboxylation gave 3,4,2-F2(MeCOCH2)C6H2NO2, which was converted to the title acid (I) via aniline derivative II.

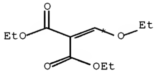
RX(23) OF 28 COMPOSED OF RX(1), RX(2), RX(3), RX(4), RX(5)
RX(23) A + B + P ===> R



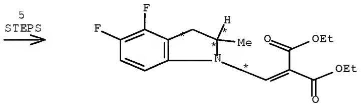
A



B



P



R
YIELD 92%

RX(1) RCT A 141-97-9, B 771-69-7

STAGE(1)
RGT D 7646-69-7 NaH
SOL 109-99-9 THF

STAGE(2)
RGT E 7647-01-0 HCl, F 64-19-7 AcOH
SOL 7732-18-5 Water

PRO C 121247-16-3

RX(2) RCT C 121247-16-3
RGT J 16940-66-2 NaBH4
PRO I 121247-17-4
SOL 67-56-1 MeOH

RX(3) RCT I 121247-17-4
RGT M 1333-74-0 H2
PRO L 121247-18-5
CAT 7440-02-0 Ni

```
          SOL  64-17-5 EtOH

RX(4)     RCT  L 121247-18-5, P 87-13-8
          PRO  Q 121247-19-6

RX(5)     RCT  Q 121247-19-6
          RGT  S 603-35-0 PPh3, T 1972-28-7 EtO2CN:NCO2Et
          PRO  R 121247-20-9
          SOL  109-99-9 THF
```

L48 ANSWER 13 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 109:190280 CASREACT Full-text

TITLE: Novel quinolone chemotherapeutics. II. Thieno[3,2-g]quinoline- and [1]benzothieno[5,6,7-ij]quinolizinecarboxylic acids

AUTHOR(S): Sauter, F.; Jordis, U.; Tanyolac, S.; Martinek, P.

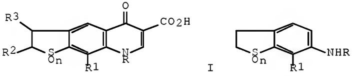
CORPORATE SOURCE: Inst. Org. Chem., Tech. Univ. Wien, Vienna, A-1060, Austria

SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1988), 321(4), 241-6
CODEN: ARPMAS; ISSN: 0365-6233

DOCUMENT TYPE: Journal

LANGUAGE: German

GI

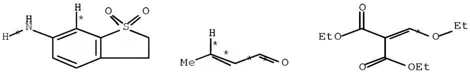


I II

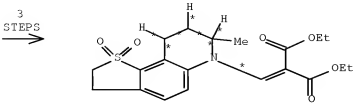
AB The title compds. I [R = H, Et, Me, Ac, R1 = H; RR1 = (CH2)3, CHMeCH2CH2; R2 = R3 = H; n = 0,1,2] were prepared by cyclizing benzothiophenes II with EtOCH:C(CO2Et)2 and ester hydrolysis. In come cases the 2,3-didehydro analogs I(R2R3 = bond) were also obtained. I (RR1 = CHMeCH2CH2, R2R3 = bond) had considerable bactericidal activity against gram-pos. organisms.

RX(70) OF 125 COMPOSED OF RX(2), RX(3), RX(7)

RX(70) D + E + M ===> R



D E M



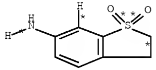
R
YIELD 66%

```
RX(2)      RCT  D 20503-39-3, E 4170-30-3
           RGT  G 7647-01-0 HCl
           PRO  F 117080-76-9

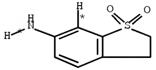
RX(3)      RCT  F 117080-76-9
           RGT  I 1333-74-0 H2
           PRO  H 117080-77-0
           CAT  7440-02-0 Ni
           SOL  108-88-3 PhMe
           NTE  Raney Ni

RX(7)      RCT  H 117080-77-0, M 87-13-8
           PRO  R 117080-80-5

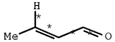
RX(77) OF 125 COMPOSED OF RX(2), RX(3), RX(26), RX(11)
RX(77)     2 D  +  2 E  +  M  ===>  Z
```



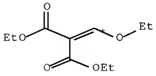
D



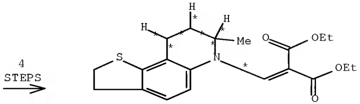
D



2 E



M



Z
YIELD 80%

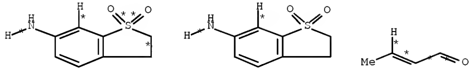
RX(2) RCT D 20503-39-3, E 4170-30-3
RGT G 7647-01-0 HCl
PRO F 117080-76-9

RX(3) RCT F 117080-76-9
RGT I 1333-74-0 H2
PRO H 117080-77-0
CAT 7440-02-0 Ni
SOL 108-88-3 PhMe
NTE Raney Ni

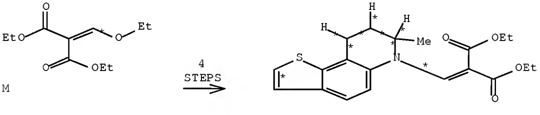
RX(26) RCT H 117080-77-0
RGT AW 1191-15-7 AlH(Bu-i)2
PRO Y 117080-98-5, L 117080-99-6
SOL 123-91-1 Dioxane

RX(11) RCT Y 117080-98-5, M 87-13-8
PRO Z 117080-84-9

RX(79) OF 125 COMPOSED OF RX(2), RX(3), RX(26), RX(12)
RX(79) 2 D + 2 E + M ===> AA



D D 2 E



M

AA
YIELD 80%

RX(2) RCT D 20503-39-3, E 4170-30-3
RGT G 7647-01-0 HCl
PRO F 117080-76-9

RX(3) RCT F 117080-76-9
RGT I 1333-74-0 H2
PRO H 117080-77-0
CAT 7440-02-0 Ni
SOL 108-88-3 PhMe

NTE Raney Ni

RX(26) RCT H 117080-77-0
RGT AW 1191-15-7 AlH(Bu-i)2
PRO Y 117080-98-5, L 117080-99-6
SOL 123-91-1 Dioxane

RX(12) RCT L 117080-99-6, M 87-13-8
PRO AA 117080-85-0

L48 ANSWER 14 OF 16 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 102:203920 CASREACT Full-text

TITLE: Synthesis of antimicrobial agents. VII. Synthesis and antibacterial activities of furo[2,3-g]quinoline derivatives

AUTHOR(S): Tanaka, Yoshiaki; Suzuki, Norio; Hayakawa, Isao; Suzuki, Kazunori

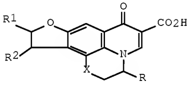
CORPORATE SOURCE: Res. Inst., Daiichi Seiyaku Co., Ltd., Tokyo, 134, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1984), 32(12), 4923-8
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

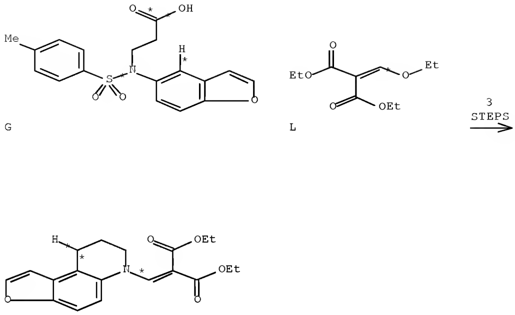


I

AB Furo[2,3-g]quinolines I (R = H, Me; R1 = R2 = H, R1R2 = bond; X = CH2,O) were synthesized, and their antibacterial activities were examined Among them, I (R = Me, R1R2 = bond, X = O) exhibited the most potent antibacterial activity against Gram-pos. and -neg. organisms, including Pseudomonas aeruginosa, and it showed low acute toxicity to mice.

RX(31) OF 49 COMPOSED OF RX(3), RX(4), RX(5)

RX(31) G + L ===> M



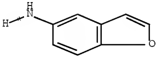
M
YIELD 55%

```
RX(3)      RCT  G 73846-19-2
           RGT  I 10026-13-8 PCl5
           PRO  H 96439-80-4

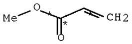
RX(4)      RCT  H 96439-80-4
           RGT  K 16853-85-3 LiAlH4
           PRO  J 96439-82-6

RX(5)      RCT  J 96439-82-6, L 87-13-8
           PRO  M 96439-81-5

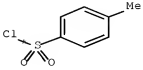
RX(32) OF 49 COMPOSED OF RX(2), RX(3), RX(4), RX(5)
RX(32)     D  +  E  +  F  +  L  ===>  M
```



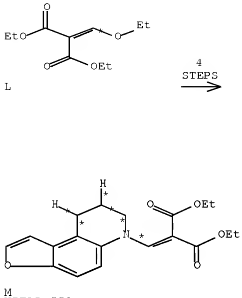
D



E



F



M
YIELD 55%

```
RX(2)       RCT   D 58546-89-7, E 96-33-3, F 98-59-9
            PRO   G 73846-19-2

RX(3)       RCT   G 73846-19-2
            RGT   I 10026-13-8 PCl5
            PRO   H 96439-80-4

RX(4)       RCT   H 96439-80-4
            RGT   K 16853-85-3 LiAlH4
            PRO   J 96439-82-6

RX(5)       RCT   J 96439-82-6, L 87-13-8
            PRO   M 96439-81-5
```

L48 ANSWER 15 OF 16 CASREACT

ACCESSION NUMBER: 99:138964 CASREACT Full-text

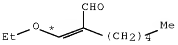
TITLE: Vinyl analog of the Vilsmeier formylation with 3-(dimethylamino)acroleins

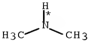
AUTHOR(S): Ullrich, F. W.; Breitmaier, E.
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Univ. Bonn, Bonn, D-5300, Fed. Rep. Ger.

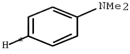
SOURCE: Synthesis (1983), (8), 641-5
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: German

AB Treatment of PhNMe2, pyrrole, or N-methylpyrrole with Me2NCH:CRCHO (I; R = H, Me, Et, Pr, pentyl) in the presence POCl3 gave 13-61% (E)-R1CH:CRCHO (R = same, R1 = p-Me2NC6H4, 2-pyrrolyl or 1-methyl-2-pyrrolyl). The I were prepared by dimethylaminolysis of EtOCH:CRCHO.

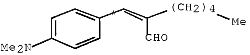
RX(15) OF 22 COMPOSED OF RX(2), RX(11)
RX(15)   E + F + B ===> U


E


F

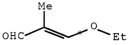

B

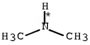
2
STEPS
→

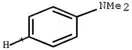

U
YIELD 21%

RX(2)	RCT	E 30989-79-8, F 124-40-3
	PRO	G 57202-65-0
RX(11)	RCT	G 57202-65-0, B 121-69-7
	RGT	D 10025-87-3 POCl3
	PRO	U 344740-58-5

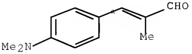
RX(16) OF 22 COMPOSED OF RX(3), RX(8)
RX(16)   H + F + B ===> R


H


F


B

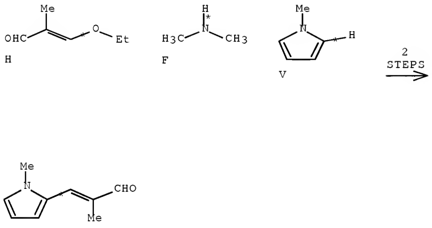
2
STEPS
→


R
YIELD 61%

```
RX(3)      RCT  H 42588-57-8, F 124-40-3
           PRO  I 19125-76-9

RX(8)      RCT  I 19125-76-9, B 121-69-7
           RGT  D 10025-87-3 POCl3
           PRO  R 181381-18-0


RX(17) OF 22 COMPOSED OF RX(3), RX(12)
RX(17)     H  +  F  +  V  ===>  W
```

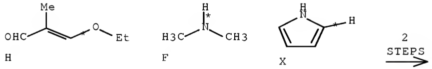


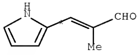
W
YIELD 13%

```
RX(3)      RCT  H 42588-57-8, F 124-40-3
           PRO  I 19125-76-9

RX(12)     RCT  I 19125-76-9, V 96-54-8
           RGT  D 10025-87-3 POCl3
           PRO  W 87234-32-0


RX(18) OF 22 COMPOSED OF RX(3), RX(13)
RX(18)     H  +  F  +  X  ===>  Y
```



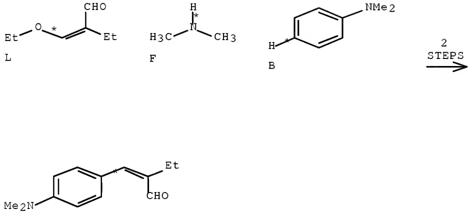


Y
YIELD 51%

RX(3)   RCT   H 42588-57-8, F 124-40-3
            PRO   I 19125-76-9

RX(13)   RCT   I 19125-76-9, X 109-97-7
            RGT   D 10025-87-3 POCl3
            PRO   Y 49616-04-8

RX(21) OF 22 COMPOSED OF RX(5), RX(9)
RX(21)   L + F + B ===> S

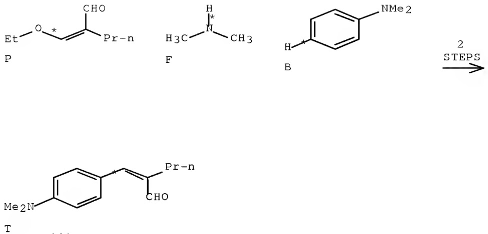


S
YIELD 37%

RX(5)   RCT   L 30989-75-4, F 124-40-3
            PRO   M 38062-54-3

RX(9)   RCT   M 38062-54-3, B 121-69-7
            RGT   D 10025-87-3 POCl3
            PRO   S 87234-34-2

RX(22) OF 22 COMPOSED OF RX(7), RX(10)
RX(22)   P + F + B ===> T



YIELD 32%

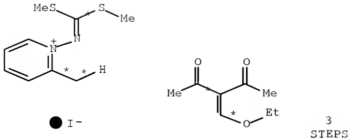
RX(7)   RCT   P 21037-71-8, F 124-40-3
           PRO   Q 87234-37-5

RX(10)   RCT   Q 87234-37-5, B 121-69-7
           RGT   D 10025-87-3 POCl3
           PRO   T 345640-33-7

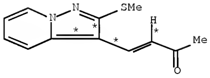
L48 ANSWER 16 OF 16 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 93:239303 CASREACT Full-text
TITLE: Synthesis using allylidenedihydropyridines. VIII. Facile preparation of 2-(alkylthio)-3-vinylpyrazolo[1,5-a]pyridines
AUTHOR(S):   Kakehi, Akikazu; Ito, Suketaka; Watanabe, Kozo
CORPORATE SOURCE: Fac. Eng., Shinshu Univ., Nagano, 380, Japan
SOURCE: Bulletin of the Chemical Society of Japan (1980), 53(6), 1775-6
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB   Reactions of 1-[bis(alkylthio)methyleneamino]-2-methylpyridinium iodides with activated ethoxymethylene compds. in the presence of alkali gave the corresponding 1-[bis(alkylthio)methyleneamino]-2-allylidene-1,2-dihydropyridines in considerable yields, and their thermolyses in benzene afforded 2-alkylthio-3-vinylpyrazolo[1,5-a]pyridine derivs.

RX(26) OF 28 COMPOSED OF RX(5), RX(8), RX(10)
RX(26)   B + L ===> T



H L 3 STEPS



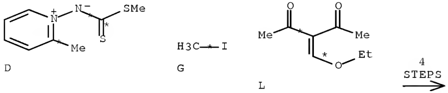
T
YIELD 65%

```
RX(5)      RCT  H 75619-83-9, L 33884-41-2
           PRO  M 75619-86-2
           CAT  584-08-7 K2CO3

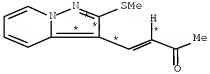
RX(8)      RCT  M 75619-86-2
           PRO  Q 75619-89-5

RX(10)     RCT  Q 75619-89-5
           RGT  U 7647-01-0 HCl
           PRO  T 75619-92-0
```

RX(27) OF 28 COMPOSED OF RX(3), RX(5), RX(8), RX(10)
RX(27)   D + G + L ===> T



D G L 4 STEPS



T
YIELD 65%

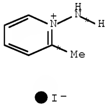
```
RX(3)      RCT  D 75619-82-8, G 74-88-4
           PRO  H 75619-83-9

RX(5)      RCT  H 75619-83-9, L 33884-41-2
           PRO  M 75619-86-2
           CAT  584-08-7 K2CO3

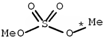
RX(8)      RCT  M 75619-86-2
           PRO  Q 75619-89-5

RX(10)     RCT  Q 75619-89-5
           RGT  U 7647-01-0 HCl
           PRO  T 75619-92-0

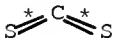

RX(28) OF 28 COMPOSED OF RX(1), RX(3), RX(5), RX(8), RX(10)
RX(28)     A  +  B  +  C  +  G  +  L  ===>  T
```



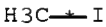
A



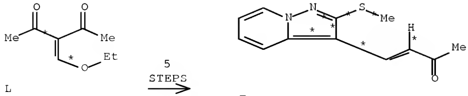
B



C



G



L

T
YIELD 65%

```
RX(1)     RCT  A 7583-90-6, B 77-78-1, C 75-15-0
          PRO  D 75619-82-8
          SOL  75-15-0 CS2

RX(3)     RCT  D 75619-82-8, G 74-88-4
          PRO  H 75619-83-9

RX(5)     RCT  H 75619-83-9, L 33884-41-2
          PRO  M 75619-86-2
          CAT  584-08-7 K2CO3

RX(8)     RCT  M 75619-86-2
          PRO  Q 75619-89-5

RX(10)    RCT  Q 75619-89-5
          RGT  U 7647-01-0 HCl
          PRO  T 75619-92-0
```

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=> d his full

     (FILE 'HOME' ENTERED AT 13:52:54 ON 08 SEP 2008)

     FILE 'REGISTRY' ENTERED AT 13:53:56 ON 08 SEP 2008

     FILE 'CASREACT' ENTERED AT 13:54:23 ON 08 SEP 2008
                ACT BIA486STRL15/A
               ---------
L1              STR
L2  (     190274)SEA ABB=ON  PLU=ON  ACYCLIC ALKENE/FG.PRO
L3              SCR 278 OR 1342
L4           143 SEA SUB=L2 SSS FUL L1 AND L3 (   742 REACTIONS)
               ---------
L5              STRUCTURE UPLOADED
L6             3 SEA SUB=L4 SSS SAM L5 (     90 REACTIONS)
L7            43 SEA SUB=L4 SSS FUL L5 (    207 REACTIONS)

     FILE 'REGISTRY' ENTERED AT 13:56:43 ON 08 SEP 2008

     FILE 'CASREACT' ENTERED AT 13:56:57 ON 08 SEP 2008
L8              TRA PLU=ON  L4 1- RX :     1312 TERMS

     FILE 'REGISTRY' ENTERED AT 13:57:35 ON 08 SEP 2008
L9          1312 SEA ABB=ON  PLU=ON  L8/RN
L10          441 SEA ABB=ON  PLU=ON  L9 AND X/ELS
L11          421 SEA ABB=ON  PLU=ON  L10 AND C/ELS
L12           20 SEA ABB=ON  PLU=ON  L10 NOT L11

     FILE 'CASREACT' ENTERED AT 13:58:10 ON 08 SEP 2008
L13       188275 SEA ABB=ON  PLU=ON  L12
L14           24 SEA ABB=ON  PLU=ON  L13 (L) L7
L15           48 SEA ABB=ON  PLU=ON  L13 (L) L4

     FILE 'REGISTRY' ENTERED AT 13:59:03 ON 08 SEP 2008
L16           11 SEA ABB=ON  PLU=ON  L12 AND M/ELS
L17            9 SEA ABB=ON  PLU=ON  L12 NOT L16
                D SCA

     FILE 'CASREACT' ENTERED AT 13:59:43 ON 08 SEP 2008
L18       153759 SEA ABB=ON  PLU=ON  L17
L19           31 SEA ABB=ON  PLU=ON  L18 (L) L4
L20           40 SEA ABB=ON  PLU=ON  L19 OR L14
L21           15 SEA ABB=ON  PLU=ON  L19 AND L14
L22           16 SEA ABB=ON  PLU=ON  L19 NOT L14
                D OCC
                D OCC 1-16
                D OCC L14 TOT

     FILE 'CAPLUS' ENTERED AT 14:03:23 ON 08 SEP 2008
L23        30349 SEA ABB=ON  PLU=ON  WANG W?/AU
L24          645 SEA ABB=ON  PLU=ON  IKEMOTO T?/AU
L25            8 SEA ABB=ON  PLU=ON  L23 AND L24

     FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:04:23 ON 08 SEP 2008
L26            9 SEA ABB=ON  PLU=ON  L25

     FILE 'CAPLUS' ENTERED AT 14:04:46 ON 08 SEP 2008
```

```
L27           24 SEA ABB=ON  PLU=ON  L14
L28           15 SEA ABB=ON  PLU=ON  L21
L29           16 SEA ABB=ON  PLU=ON  L22
L30            1 SEA ABB=ON  PLU=ON  (L23 OR L24) AND (L27 OR L28 OR L29)
L31          143 SEA ABB=ON  PLU=ON  L4
L32            1 SEA ABB=ON  PLU=ON  L31 AND (L23 OR L24)
                 SEL AN

     FILE 'CASREACT' ENTERED AT 14:05:39 ON 08 SEP 2008
L33            1 SEA ABB=ON  PLU=ON  ("143:78029"/AN OR "2005:378843"/AN)
L34           40 SEA ABB=ON  PLU=ON  L14 OR L21 OR L22
L35            1 SEA ABB=ON  PLU=ON  L34 AND L33
                 D HIT

     FILE 'REGISTRY' ENTERED AT 14:06:39 ON 08 SEP 2008
L36            1 SEA ABB=ON  PLU=ON  ACETIC ACID/CN
                 D RN

     FILE 'CASREACT' ENTERED AT 14:06:51 ON 08 SEP 2008
L37        75833 SEA ABB=ON  PLU=ON  64-19-7
L38           16 SEA ABB=ON  PLU=ON  L37 (L) L4
L39           14 SEA ABB=ON  PLU=ON  L37 (L) L34
L40            2 SEA ABB=ON  PLU=ON  L37 (L) L14
L41            4 SEA ABB=ON  PLU=ON  L37 (L) L21
L42           10 SEA ABB=ON  PLU=ON  L37 (L) L22
L43            7 SEA ABB=ON  PLU=ON  L37 (L) L19

     FILE 'CAPLUS' ENTERED AT 14:08:44 ON 08 SEP 2008
                 D STAT QUE L25

     FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:08:55 ON 08 SEP 2008
                 D STAT QUE L29

     FILE 'CAPLUS' ENTERED AT 14:09:16 ON 08 SEP 2008
L44           24 DUP REM L25 L29 (0 DUPLICATES REMOVED)
                      ANSWERS '1-24' FROM FILE CAPLUS

     FILE 'REGISTRY' ENTERED AT 14:10:17 ON 08 SEP 2008

     FILE 'CAPLUS' ENTERED AT 14:10:19 ON 08 SEP 2008
                 D STAT QUE L25

     FILE 'MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:10:32 ON 08 SEP 2008
                 D STAT QUE L26

     FILE 'CAPLUS, EMBASE, WPIX' ENTERED AT 14:10:43 ON 08 SEP 2008
L45           10 DUP REM L25 L26 (7 DUPLICATES REMOVED)
                      ANSWERS '1-8' FROM FILE CAPLUS
                      ANSWERS '9-10' FROM FILE WPIX
                 D IBIB ABS L45 1-8
                 D IALL L45 9-10

     FILE 'CASREACT' ENTERED AT 14:11:16 ON 08 SEP 2008
                 D STAT QUE L14
                 D STAT QUE L40
                 D STAT QUE L21
L46           24 SEA ABB=ON  PLU=ON  L14 OR L40 OR L21
                 D IBIB ABS HIT L46 1-24

     FILE 'REGISTRY' ENTERED AT 14:17:10 ON 08 SEP 2008
```

```
     FILE 'CASREACT' ENTERED AT 14:17:14 ON 08 SEP 2008
                D STAT QUE L22
                D STAT QUE L43
L47          18 SEA ABB=ON  PLU=ON  L22 OR L43
L48          16 SEA ABB=ON  PLU=ON  L47 NOT L46
                D IBIB ABS HIT L48 1-16
```

FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

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STRUCTURE FILE UPDATES:    7 SEP 2008  HIGHEST RN 1047406-12-1
DICTIONARY FILE UPDATES:   7 SEP 2008  HIGHEST RN 1047406-12-1
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE CASREACT

FILE CONTENT:1840 - 31 Aug 2008 VOL 149 ISS 10

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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*******************************************************
*                                                            *
*     CASREACT now has more than 15.3 million reactions     *
*                                                            *
*******************************************************
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FILE CAPLUS

FILE COVERS 1907 - 8 Sep 2008 VOL 149 ISS 11
FILE LAST UPDATED: 7 Sep 2008 (20080907/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

FILE MEDLINE
FILE LAST UPDATED: 7 Sep 2008 (20080907/UP). FILE COVERS 1949 TO DATE.

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

MEDLINE Accession Numbers (ANs) for records from 1950-1977 have been converted from 8 to 10 digits. Searches using an 8 or 10 digit AN will retrieve the same record. The 10-digit ANs can be expanded, searched, and displayed in all records from 1949 to the present.

FILE EMBASE
FILE COVERS 1974 TO 8 Sep 2008 (20080908/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 3 September 2008 (20080903/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE WPIX
FILE LAST UPDATED: 3 SEP 2008 <20080903/UP>
MOST RECENT UPDATE: 200856 <200856/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> Now containing more than 1.1 million chemical structures in DCR <<<

>>> IPC Reform backfile reclassifications have been loaded to the end of June 2008. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC, 20071130/UPIC, 20080401/UPIC and 20080701/UPIC. ECLA reclassifications to June and US national classifications to the end of April 2008 have also been loaded. Update dates 20080401 and 20080701/UPEC and /UPNC have been assigned to these. <<<

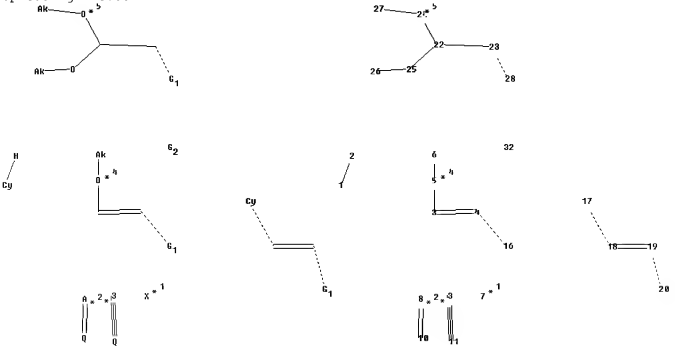
FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomsonreuters.com/support/patents/coverage/latestupdate

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.p

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

Uploading L1c.str



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chain nodes :
1  2  3  4  5  6  7  16  17  18  19  20  22  23  24  25  26  27  28  32
ring/chain nodes :
8  9  10  11
chain bonds :
1-2  3-4  3-5  4-16  5-6  17-18  18-19  19-20  22-23  22-24  22-25  23-28  24-27
25-26
ring/chain bonds :
8-10  9-11
exact/norm bonds :
1-2  3-5  4-16  5-6  8-10  9-11  17-18  19-20  22-24  22-25  23-28  24-27  25-26

exact bonds :
3-4  18-19  22-23


G1:[*1],[*2],[*3]

G2:[*4],[*5]

Match level :
1:Atom  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS
11:CLASS  16:CLASS  17:Atom  18:CLASS  19:CLASS  20:CLASS  22:CLASS  23:CLASS
24:CLASS  25:CLASS
26:CLASS  27:CLASS  28:CLASS  32:CLASS
Generic attributes :
1:
Saturation             : Unsaturated
17:
Saturation             : Unsaturated

fragments assigned reactant role:
containing 1
containing 32
fragments assigned product role:
containing 17
reaction site bonds:
17-18:CC



Uploading L5c.str
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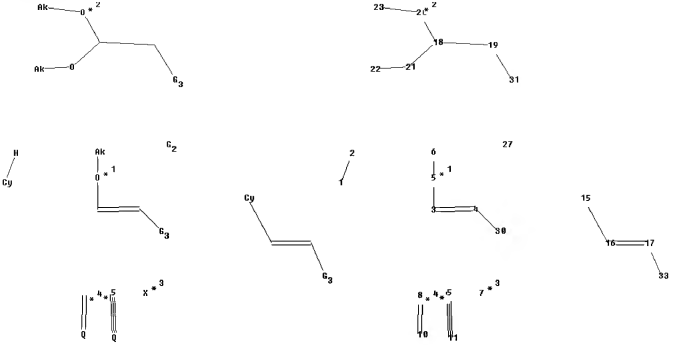

chain nodes :
1 2 3 4 5 6 7 8 9 10 11 15 16 17 18 19 20 21 22 23 27 30 31
33
chain bonds :
1-2 3-4 3-5 4-30 5-6 8-10 9-11 15-16 16-17 17-33 18-19 18-20 18-21 19-
31
20-23 21-22
exact/norm bonds :
1-2 3-5 4-30 5-6 8-10 9-11 15-16 17-33 18-20 18-21 19-31 20-23 21-22

exact bonds :
3-4 16-17 18-19

G2:[*1],[*2]

G3:[*3],[*4],[*5]

Hydrogen count :
3:= exact 1 4:= exact 1 16:= exact 1 17:= exact 1 18:= exact 1 19:= exact 2

Connectivity :
3:2 E exact RC ring/chain 4:2 E exact RC ring/chain 16:2 E exact RC ring/chain
17:2 E exact RC ring/chain 18:3 E exact RC ring/chain 19:2 E exact RC ring/chain
Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS
11:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS
27:CLASS 30:CLASS 31:CLASS 33:CLASS
Generic attributes :
1:
Saturation : Unsaturated
15:
Saturation : Unsaturated

```
fragments assigned reactant role:
containing 1
containing 27
fragments assigned product role:
containing 15
reaction site bonds:
15-16:CC



=>
```